BRAIN

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A Journal of Neurology

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BRAIN

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GENERAL PRINCIPLES OF NERVOUS ACTIVITY.

(Hughlings Jackson Lecture.[1])

BY

E. D. ADRIAN.

FEW of the present generation could give an adequate account of the doctrines of Herbert Spencer. His name is rarely seen in the lists of eminent philosophers, biologists or sociologists, and if we know anything of his work our knowledge is probably at second hand. Yet eighty years ago Spencer influenced the thought of the whole civilized world, as profoundedly as his antithesis, Lord Byron, had done a generation earlier. At his death in 1903 the Italian Chamber adjourned as a sign of condolence, and the whole Continent blamed us for not giving enough recognition to his greatness. He preached the new creed of science when other creeds were losing their appeal, and it was still a time when it seemed possible for one man to write with authority on most of natural knowledge. Whewell, the famous Master of Trinity, had done so before him, but Whewell combined encyclopædic learning with a real understanding of physical ideas. Spencer had a less rigorous outlook: his first principles were far more accommodating than the laws of Nature had any right to be for they explained the whole history of the world and of mankind as the logical consequence of the Persistence of Force, the Instability of the Homogeneous, the evolution of the Heterogeneous, leading to Segregation, Equilibrium and finally to Dissolution. This kind of system building by deduction was still in fashion: Hegel and his disciples had built up a far less reasonable world on far more abstract principles, but Spencer's formula was easier to understand and so much more vulnerable. The next generation would not have it. The formula had lost its appeal and James Ward's attack was the end.

Yet a whole generation of the civilized world, even a mid-Victorian generation, is not influenced for nothing. Spencer had given it new ideas

[1] Delivered on January 2, 1947.

which we take for granted nowadays. His influence appears in many fields of knowledge developed in the last century and it appears particularly in the field of neurology.

We can afford to remain ignorant of most of Herbert Spencer's abstract biological doctrines, but not of the neurological doctrines of his great admirer, Hughlings Jackson. His theories and predictions, based on Spencer, illuminated the study of the nervous system and the illumination is as brilliant as ever. One reason, no doubt, is that Hughlings Jackson had a wide range of facts demanding some relatively simple framework to contain them. They showed the faulty working of a nervous organization about which very little was known, and Jackson could use the general ideas of evolution and dissolution to give them meaning. The other reason is that he was a scientific observer of the first rank, forever anxious to understand the "nature" of the phenomena he observed. His writings show the difference between his approach and that of his model. They are still fresh and individual, none the worse for advancing knowledge and all the better for their peculiarities. The copious footnotes and sub-headings, the concern that his meaning should not be misinterpreted, the speculations which so often hit the nail on the head,[1] these fill in a lively picture of the physician-philosopher who founded the British School of Neurology, and it is far more attractive than the picture of dreary self-absorption which Spencer left in his autobiography.

The guiding principles of Jackson's system have been so well expounded that there can be no need to recapitulate them. They rest on the idea of three main levels of organization in the central nervous system, on its mode of evolution and consequent mode of dissolution and on the positive and negative symptoms which follow. His ideas are cast in terms so general that they would apply whatever the detailed structure of the nervous system might be. Most of them were published before the neurone theory was formulated: his sensory and motor elements and the units of which he speaks are not necessarily the units of the cytologist—the neurone with its single axon—for though he had most of the data of clinical neurology as we have them now he had not the great mass of detailed information about cell structure or cell physiology under which we labour. We have no Spencer to give us an accommodating framework

[1] Since footnotes are surely admissible in a Hughlings Jackson lecture electroencephalographers may be interested in this remark on epilepsy. "I suppose before the abrupt explosion which constitutes the severe fit there are frequent minute discharges—too trivial to produce any visible effects." "Selected Writings." Vol. 1, p. 16.

and no Hughlings Jackson to fill in the picture: but we ought to try from time to time to survey our new knowledge with Hughlings Jackson's example in mind, not so much in the pious attempt to make them fit his scheme but in the expectation that we shall learn something by so doing.

Reflex levels.—He makes three statements about the evolution of the nervous system which can be taken as a starting point. Evolution, he says: (1) Is a passage from the most to the least organized; that is, from the lowest, well-organized centres up to the highest, least organized centres; (2) it is a passage from the most simple to the most complex; and (3) from the most automatic to the most voluntary. He points out in the same passage that there is no inconsistency in speaking of centres being at the same time most complex and least organized, for in a centre of two sensory and two motor elements well joined, currents will flow easily from the sensory into the motor units, so that the centre, although very simple, is well organized. On the other hand, in a centre of four sensory and four motor elements imperfectly joined, the flow may meet with much more resistance and the organization will, therefore, be less although the centre is more complex.

It happens that recent neurophysiology has given us some fairly straightforward examples of centres or pathways of varying complexity, and it may be interesting to review them in the light of Jackson's scheme. The stretch reflex is an example of a very simple type of nervous mechanism and an illustration of the interaction of different levels on which Jackson insisted. Its simplicity and high degree of organization in Jackson's sense was shown by Liddell and Sherrington's analysis. The response follows the stimulus with a correspondence almost as close as in an isolated muscle nerve preparation. There is no after-discharge and no increasing spread to other muscles: the only difference is its dependence on the activity of the postural centres in the mid-brain. The reflex arc is as simple as it can be. Hoffmann (1922), studying stretch reflex phenomena in man, suggested that only two neurones were involved, for Cajal had shown that there were collaterals from some of the afferent fibres passing through the grey matter of the cord to the motor nerve cells. Lloyd (1943) and Renshaw (1940) have now measured the synaptic delay in the pathway of this and other reflexes and they find that for the stretch reflex the delay is only 0·6 m.sec., that characteristic of a single synaptic junction.

The stretch reflex is, therefore, an example of the lowest level of nervous complexity and the highest degree of organization, but it is at the service of the higher levels which can adjust the degree of synaptic resis-

tance, i.e. the intensity of the afferent discharge needed to break through. It could not be used to regulate posture and movement if it were less highly organized (or canalized), for the contractions of different muscles must be accurately adjusted to the different tensions in them. There are many other examples of such direct, through connection in other parts of the nervous system; at relay stations on the long ascending tracts for instance, where this kind of organization allows the convergence of many afferent pathways on to one efferent.

In the flexion reflex, the response to pain, we find a higher level of complexity. The synaptic delay is 1·2 m.sec., the arc, therefore, has at least three neurones, and the intermediate neurones form a spreading network. The motor discharge is no longer rigidly confined to the one pathway and is no longer a precise copy of the afferent discharge. Again, the reflex would have little value without these properties. The painful stimulus must be avoided if the body is to escape damage and if the danger signals persist and increase, the avoiding movements must become more powerful, involving more and more muscles. The power of evoking intense and widespread activity is now much more important than precise localization, and it is conferred by the less definitely organized arrangement in which the afferent discharge has access to a whole network of internuncial neurones allowing for divergence of the effect as well as convergence. As Sherrington pointed out, the reflex displays some degree of "inertia" and "momentum," though not so much as in the crossed extension reflex. The response is no longer a faithful copy of the stimulus and there is some hint of the much greater lack of correspondence which we find at higher levels.

Persistence of central activity.—When we come to inquire what is actually happening in the neurones involved in these reflexes we begin to enter the realm of speculation. An important feature, perhaps the most important feature, of synaptic conduction is its variable time course. In the flexion reflex an afferent discharge lasting one second may give an efferent ten times as long, and as we go to higher levels the evidence of long-lasting central effects becomes more and more striking, culminating in the cerebrum, where the results of an afferent message can be stored indefinitely to influence behaviour many years later. In the nerve fibre the chief manifestation of activity is the very brief self-quenching wave of excitation which constitutes the nerve impulse. Are any other kinds of activity likely to occur in the central regions to account for the slower effects?

We have really two manifestations of central activity to explain. In

the lower levels there is the inertia and momentum, the slower rise and the after-discharge when the afferent signal is over; and in the higher levels there is also a tendency to continued cell activity, to rhythmic pulsation modified by, but not obviously in phase with, afferent signals. The evidence for this depends on electrical changes rather than on motor effects, but it is clearly an important feature of the cerebral organization.

Recent neurophysiology has developed two divergent hypotheses to account for these features of central activity. That associated with Lorente de No and Lloyd has the advantage of relating both properties to a single cause—the widespread connections formed by the dendrites of internuncial neurones. On this view protracted discharges from the spinal cord are thought of as the result, not of a protracted and continuous stimulus to the nerve cells, but of a continued bombardment of the motor neurones by impulses which reach them from multiple pathways. Pathways with different conduction time (delay paths) will cause the impulses from a single afferent volley to arrive successively instead of simultaneously. This will account for the after-discharge; and an extension of the idea will account also for the persistent rhythmic activities of the higher centres, for self-exciting circuits may be set going in the dendrite network and these will send on an impulse whenever the cycle recurs.

The idea is attractive because it can be made to explain so many different features of central activity. There is histological sanction for pathways of all degrees of complexity, and the properties ascribed to them are reasonable. They may well act as they are supposed to do, but there is very little direct evidence of such extreme brevity in central stimulation and no convincing proof of the importance of reverberating circuits in the higher levels. Moreover, there is considerable evidence for quite another kind of central activity. In 1938 Barron and Matthews found that an afferent volley entering the spinal cord would set up a potential change of definite but much longer time relations which could be detected most easily in the dorsal roots but was certainly derived from the grey matter of the cord. These electrical effects show the summation and relatively slow decline which used to be credited to the hypothetical "central excitatory state." They resemble the potentials developed in various nerve ganglia and at the motor nerve endings, and it is natural to regard them as an index of the stimulating effect of one neurone on another. Their relation to the positive and negative after-potentials (which follow activity in nerve) is still not certain, but if we can accept them as evidence of semi-persistent central activity, the delay paths and reverberating circuits become less important.

If central excitations can be maintained and can rise and fall in intensity as these potential changes suggest, it is certainly easier to account for the regular rhythms of discharge from the motor neurones, rhythms which rise and fall like those from an excited sense organ. These are not readily explained as a consequence of bombardment by brief impulses, but Barron and Matthews (1938) found that a small current passed through the cord would produce a typical rhythmic discharge from the ventral roots, and they showed that the potentials developed by afferent activity should have the same kind of stimulating effect. Granit (1946) has made use of the same idea in his studies of the retinal discharge, and Hodgkin, working on single crustacean nerve fibres, has shown how the rhythm may be determined by a gradual rebuilding of the local excitatory state after each impulse has been discharged. Bremer (1940) and, more recently, Eccles (1946) have extended the analysis of the root potentials and confirmed their properties.

We are on fairly firm ground, therefore, in assuming that the passage of excitation from one neurone to the next can involve slower changes than the nerve impulse and that considerable electrical effects may accompany these changes. Whether we must reckon with the liberation of substances like acetylcholine, as we must do at the motor nerve ending, is still very uncertain; but humoral agent or end-plate potential, there is reason to believe that the central stimulus can be made to persist as a relatively steady state as long as a train of afferent impulses continues.

Electrical interaction.—Part of the importance of Barron and Matthew's work lies in its bearing on the potentials which we can record from the surface of the brain. The relatively slow waves of the α rhythm, for instance, may well be generated as local dendrite potentials like those in the cord, and we may be able to subject them to the same kind of analysis. Another point of importance is that we can detect them at some distance from their source, and if our amplifiers can do so it is possible that the nerve cells can do so too. The spread of excitation through a mass or sheet of nerve cells is certainly guided to a great extent by the pathways formed by dendrites in close contact; but it is possible that besides these relatively insulated, well-organized pathways, the more diffuse connections of the higher levels may depend to some extent on the electric fields which are generated by active areas.

The idea of the association of neurones by electric rather than direct neural influence is not new, but some fresh evidence has appeared recently. Libet and Gerard (1938) showed some years ago that the two halves of a frog's brain, completely separated by a cut and then brought into contact

might influence one another enough to give a synchronous beat. Here the activity was abnormal and the factor of injury may have contributed to the result, for injured regions lose their insulation and can certainly influence one another by electric spread. But Bremer's work (1940) on the strychnine discharge from the spinal cord leaves very little doubt that in this case the synchronization is due to electrical interaction whether injury is present or not. Another line of evidence is supplied by Arvanitaki's preparation of single complete neurones, dissected from the nerve ganglia of Aplysia (Arvanitaki, 1942). This, like the single synaptic junction and the isolated crustacean nerve fibre, is one of the newest developments of neurophysiology. Rhythmic activity often develops in the isolated neurone: if an inactive nerve cell is brought close to an active it will often begin to beat in phase with it, and if two active neurones are brought near to one another their activity may become more or less synchronous, to revert to independent rhythms when they are separated.

There are many interesting points about this mode of interaction—diffuse, covering relatively wide fields, varying in intensity with distance, &c. But the records bring us back to the second property of nerve centres, their tendency in some places to give a continued rhythmic beat. In these single neurone preparations there is no possibility of self-exciting circuits. The conditions may be abnormal, but evidently we must reckon with the fact that there are nerve cells which will not stay quiet if they are left alone, which will not remain in stable equilibrium but are constantly passing to and fro from the active to the inactive state.

Central rhythms.—Continued rhythmic activity is characteristic of the higher centres, judged by their electrical effects. And if and when it occurs it will obviously add to the complexity of the results produced when an afferent signal reaches the centres. In the cerebral cortex, for instance, we find a continual oscillation of potential regular or irregular, uniform over considerable areas or varying from place to place. Whatever its cause it means that the neurones cannot be thought of as in the same state from one moment to another; if they are not all beating together an afferent signal will find some refractory and others excitable. We find, indeed, that if afferent signals are sent in with a rhythm close to that of the cells, they may succeed in influencing a large number to beat in phase, but more often the influence will be far less obvious and will rarely succeed in making the activity of the influenced region an exact copy of that influencing it. There are certain drugs, chloralose in particular, which diminish this rhythmic tendency of the cortical neurones without interfering with their power to respond to afferent excitation. It is interesting

to find that with these the activity of the cerebral cortex loses most of its complexity and comes to resemble that of the simplest reflex level. A series of touches to the foot will now give a series of jerky contractions of the limb due to a direct spread of the cortical excitation from sensory to motor area. The cortex reverts to the low level type of response and all the normal complexity is lost (Adrian and Moruzzi, 1939).

The tendency to rhythmic activity in the neurones of the highest centres, and the possibility of influence by electrical rather than dendrite connection, are the two factors which we must bear in mind in forming a picture of the organization found in the cerebral cortex. It is an organization in which all manner of complex heterogeneous activity can occur but in which the same regions will often be found acting as a homogeneous sheet and giving a uniform beat at a high or at a low frequency.

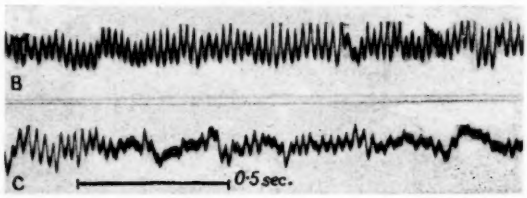

FIG. 1.—Potential waves produced by injury to the cerebral cortex (puncture with a fine wire) in a rabbit under urethane. The initial frequency was 64 per sec.; it falls to 44 per sec. in B, and finally to 40 per sec. in C (*from* Adrian and Matthews, 1934, *J. Physiol.*, **81**, 440).

Homogeneous activity.—Uniform low frequency rhythms, like the α rhythm, can only occur when the disturbing influence of afferent signals is excluded. When they are admitted the rhythm is broken up either from active inhibition or from interference with the synchronizing process, and the cortex enters on the irregular, heterogeneous activity, which is presumably necessary for discriminative behaviour. But if the excitation is intense, or if the cells are highly active, a rapid uniform rhythm may spread widely. The cells can then become associated together by relatively small synchronizing forces because at high levels of excitation the frequencies of response are all approaching to the maximum value. Since they illustrate one of the simplest ways in which cells can interact at high levels it is worth discussing the high-frequency rhythms in more detail. In the cerebrum uniform rhythmic activity with a period of 60 per sec. or more may be set up by strong electrical stimulation or by injury (fig. 1). Such a rhythm may continue for many seconds after the stimulation is

over and may spread well beyond the confines of the area stimulated. A similar rhythm often appears in light ether or chloroform anæsthesia and the waves are then increased in the receiving areas by an afferent stimulus like a touch or a sound. In the normal cerebrum, however, in the conscious and alert state heterogeneous activity is the rule. On the other hand, the cerebellum seems to be always nearer to the conditions favouring a synchronized beat. Its characteristic activity is a very rapid and regular potential rhythm with a frequency in the neighbourhood of 150-250 per sec. This is maintained by the constant inflow of afferent signals, but if an additional message is sent in the waves are increased in size and regularity, most of all at the point stimulated but to some extent in all the limb areas on that side.

The tendency to synchronous activity in the cerebellum may be due in part to the nature of the cell connections but it must certainly be favoured by the high level of activity in the cells. The normal frequency

FIG. 2.—Development of regular rhythm in the forearm flexors (E. D. A.) as the contraction increases. Record with Grass ink-writer oscillograph and pad electrodes. Final frequency = 42 per sec.

of response is not much below the maximum obtained with electric stimulation (300 per sec.), and the rhythm breaks up as soon as the frequency falls below 150 a second. All manner of cell groups show the same tendency. Whatever their structural differences we find a synchronizing effect when the excitation is intense enough to force a discharge at high rates. An old example, often neglected nowadays, is the Piper rhythm, the regular rhythm of the electrical waves in muscles contracting voluntarily with maximum effort (fig. 2). Piper may have prejudiced his case by insisting too much on a fixed frequency of 50 per sec., for fairly regular rhythms can develop at rates which vary from 35 to 60 per second. They may possibly depend on the afferent discharge from the muscle, like a clonus, but in weaker contractions where the motor units are working at lower frequencies the synchronizing effect disappears (fig. 3), and under intense excitation the neurones of the spinal cord or of the higher centres that drive them would be likely to become synchronized and to give just

such an effect. At all events there is no difficulty in recording synchronized motor discharges in the phrenic nerve when the respiratory centre is in-

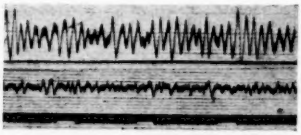

FIG. 3.—Electromyogram of forearm flexors in maximal voluntary contraction (upper record) and in weaker contraction (lower record), showing regular waves at 50 per sec. (the Piper rhythm) with maximal effort. String galvanometer records, time marker gives 0·2 sec. intervals (*from* Henriques and Lindhard, 1920, *Arch f. d. ges. Physiol.*, **183**, 1).

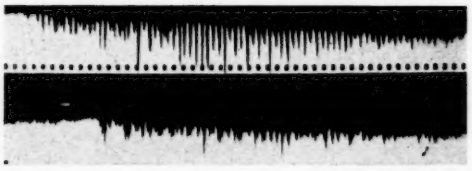

FIG. 4.—Action potentials from the top root of the phrenic nerve in a rabbit under urethane. In the upper record the airway has been obstructed and the motor neurones give a synchronous discharge at a frequency of 90 per sec. In the lower record breathing is normal and there is little synchronization.

FIG. 5.—Record from the top root of the phrenic in a decerebrate cat after a period of asphyxia, showing impulses discharged in groups at 28 per sec.

FIG. 6.—Record from the optic nerve of the water beetle (Dytiscus) with the eye moderately (B) and very brightly illuminated (C). With an intense stimulus the impulses are discharged in groups at 36 per sec. (*from* Adrian, 1937, *J. Physiol.*, **91**, 66).

tensely excited, whether afferent discharges are reaching it from the diaphragm or not. This may be seen in records from the rabbit's phrenic during forcible inspiration (fig. 4) and the grouping of the motor impulses is shown more clearly in fig. 5 which comes from the top root of the phrenic in a decerebrate cat, partially asphyxiated and so breathing with maximum effort. Compare this again with a record from an entirely different preparation, the nerve from the optic ganglion of the water beetle when the eye is brightly illuminated (fig. 6).

High-frequency synchronization could be achieved by electrical spread from one neurone to another as well as by the normal process of dendrite conduction. It is certainly due to the former when it occurs at the cut end of a nerve trunk where the insulation of the fibres has been broken down (Adrian, 1930), but in this case the interaction can sometimes be checked by placing a drop of Ringer's fluid on the cut end instead of

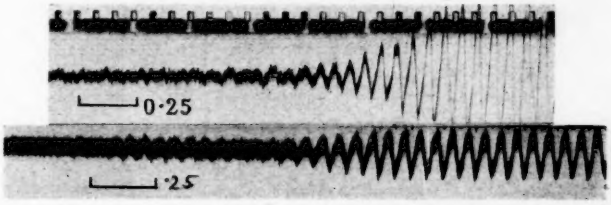

FIG. 7.—Progressive development of rhythm in the optic nerve of Dytiscus. In the upper record the eye had been brightly illuminated for 4 sec. before the rhythm developed; in the lower record for ½ sec.

leaving it exposed to the air with little conducting fluid to dissipate the currents. In the intact animal, therefore, the amount of short-circuiting may always be enough to prevent electrical interaction or at least to make it far less effective than direct conduction by dendrites. On the other hand, the influence exerted by one cell on another need not be great; it is evidently not great enough to force a uniform rhythm with minor degrees of excitation when there would be more difference in the individual response frequencies, and under intense excitation when the neurones are all responding near their maximum frequency a very small synchronizing force might start the process by bringing a few of them into phase. A gradual building up of the synchronized rhythm can often be seen (fig. 7) and the larger the group acting as pacemaker the greater the electrical effect would be.

In any case this kind of association is an example of the diffuse, poorly

organized connection which may be found in the large masses of cells of the higher levels. But in thinking in terms of spreading electrical fields we are in some danger of not thinking in terms of fixed anatomical connection. Though delay paths and reverberating circuits may not be the whole story it will not do to neglect all that is known about the histology of the cerebral cortex. For the cerebrum heterogeneous, localized, discriminative activity is essential and it must depend to a great extent on structural differences. But there is another factor, not directly related to structure, namely the greater instability of the cells at the higher levels. They are seldom at rest, they need constant supplies of oxygen and food, and periods of greater or less activity may cause prolonged changes in the very small reserves at their disposal. A disturbing stimulus may therefore produce widespread effects by altering the balance of forces acting on each element.

The fluctuating excitability which must go hand in hand with the cell rhythms is probably the chief reason for the failure of most attempts to trace recognizable patterns of excitation beyond what may be called the "arrival level" of the cerebrum. Afferent signals can be made recognizable by repeating them at a fixed frequency, touching the foot 15 times a second or exposing the eye to a flickering light. The corresponding frequency can be picked up in the cortical receiving area where the afferent connections are direct and well organized and the cells can be forced to beat at a rate dictated by the signals. We might hope to trace the rhythm further, to find groups of cells elsewhere in the brain which would resonate to that particular frequency. With stimuli repeated at much slower rates the rhythm can certainly appear on the effector side, for instance most of us find it difficult to walk out of step with a beating drum, provided its rhythm does not differ too widely from our normal rate of walking. But slow rhythms are harder to detect in a record and animals are not so prone to follow a drum. With higher frequencies and some degree of anæsthesia the pattern seems to stop at the receiving area. In the unanæsthetized human brain there is some evidence of widespread diffusion with massive stimuli, for a light flickering at particular frequencies can evoke a corresponding potential rhythm between electrodes on the vertex and the frontal region as well as in the occipital area. To produce this, however, the whole visual field must flicker brightly and the range of frequencies which can be detected in the anterior half of the brain is much more restricted than in the posterior half. There is also an occasional spread for a short distance with tactile stimuli in the animal brain. Further work on these lines may be more fruitful, but at present we can form

very little idea of the cell excitations which these rhythmic patterns may cause when they pass to the highest centres of all, the centres where they will be recognized and remembered.

Levels of cerebral activity.—It is in these centres that we must look for the neural equivalent of what goes on in the mind, for its powers of memory and problem solving, and we can scarcely expect to find out much from the very crude records of electrical activity which are available at present. Until the first door has been opened by the discovery of whatever physical change it is which corresponds to memory, it is scarcely worth speculating on what lies beyond, or where it lies. For the most part we have to be content with studying what goes in and trying to relate it to what comes out, and it is only very occasionally that the data we obtain seem to have any relevance to what the brain can actually do. And when we study what happens in the projection areas we are really at a very low level in Hughlings Jackson's sense, for the receiving areas hand on what comes into them without much alteration, and the pyramidal fibres bring about patterns of movement which are probably elaborated in regions outside the motor area (in its most restricted sense).

The difference is illustrated by electrical stimulation of the cortex. Weak stimuli at a low frequency applied to the Betz cell area in the anæsthetized brain will produce no more than a series of twitches in particular muscle groups, and the result does not seem to depend in any way on what actually happens to the limb. If one muscle is prevented from shortening the contraction does not occur in another. Contrast this direct, low level type of connection with that illustrated by Professor Graham Brown's film recording the eye movements obtained by stimulating the frontal area. Stimulating a particular point causes a lateral shift of the gaze; but now we are dealing with the movement needed for a particular result, not with the contraction of particular muscles. If the head is free the eyes remain central in their orbits and the head turns. If the head is fixed the eyes turn instead. The stimulus must have brought into being a pattern of excitation causing the shift of gaze by whatever part of the motor system is free to carry it out. Here we are at a high level, and it is worth considering what kind of patterns of cell activity we might expect to find in such a region.

Patterns of locomotion.—We have only a few hints to guide us, mostly from the lower levels. Twenty-five years ago Buddenbrook (1921) found that if the middle of the three pairs of legs of a beetle is amputated the pattern of locomotion changes immediately, so that legs which formerly moved alternately now move together and vice versa. The change is

immediate, with no time for re-learning, but it does not occur if the middle pair of legs instead of being amputated are immobilized, so that the afferent impulses can still be sent in from muscles trying to contract. Clearly the change must be determined in some way by the change of afferent pattern which follows the removal of the middle pair. As with the cortex we are dealing with an arrangement for producing movement not for making certain muscles contract: it seems to be guided by the signals resulting from the movement, and it seems to depend less on particular neural connections than on the general balance of excitations, for the movements remain well co-ordinated although the nervous connections between the various ganglia have been partially cut through by a variety of different sections.

Ten Cate (1940), who has worked on these problems recently, has found that one can go a stage further: some co-ordination between the different pairs of legs can be achieved even though all nervous connections between the ganglia are cut. The sensory stimuli to the back pair of legs arising from the movements of the front pair can then act as the co-ordinating link. The legs are kept in step by rhythmic discharges from their sense organs just as two men walking together will be kept in step by sensory cues.

When we keep in step with a companion whose pace is slightly faster or slower than ours the compulsion seems to be due to synchronizing signals from any sensory field. The noise of our companion's boots is just as effective as the sight of his legs. And in some animals at least the whole development of the walking rhythm seems to depend on the balance and rhythm of afferent signals sent in by any route which is available. Gray and Lissmann (1946) find that in the toad co-ordinated walking movements cease if the whole body and limbs are de-afferented, but remain if the afferent supply to any one spinal segment on one side is left intact. One is reminded of Lashley's rats which can find their way through a maze which they have learnt in spite of gross sensory deficiencies, and of our own powers of sensory recognition and of skilled performance which again are independent of particular pathways. Both on the sensory and on the motor side, therefore, the central processes seem to have no precise localization, no necessary connection with individual neurones.

When the incoming or outgoing routes are altered no extensive reorganization can have occurred in the centres. Grindley and Dees (1947) find that similarities in visual pattern are recognized without appreciable delay: there is an immediate reaction to the significant features of the

sensory pattern just as there is an immediate adjustment of the motor pattern in the beetle when the legs are amputated. But in a case like that of the toad with the afferent supply restricted to that from a single muscle or patch of skin there is very little left to be significant. The only features are the asymmetry of the excitation reaching the cord and the way in which it fluctuates when movement takes place.

Control by afferent pattern.—There is still no completely satisfactory scheme to account for this plasticity of the central nervous system. In general terms, however, we may suppose that it is so arranged that the lower centres can only remain in a steady condition of inactivity or unchanging activity when they are exposed to the symmetrical inflow of impulses which occurs when the body is in a normal resting position. Any new element in the afferent pattern leads to a change of central activity which continues until the balance is restored by the removal of the disturbing stimulus. In the lowest level reflexes the operation of this principle is plain enough. A rise or fall of blood-pressure changes the normal inflow of signals from the carotid sinus, and this leads directly to the compensating vasomotor adjustment which restores the pressure to its normal value. The expansion of the lungs leads directly to inhibition of the movement of inspiration, and the flexion reflex removes the limb from the painful stimulus. These examples are easy to follow because the reflexes can be regarded almost as isolated events which can occur without much disturbance to the general balance of the nervous system. At higher levels, however, the stimulus may start a train of complex activities each of which will modify the general pattern, both by the afferent signals set up by movement and by the spread of central excitations. The result is now achieved not by fixed pathways leading to particular effectors, but by general reactions causing appropriate movement. Finally at the highest level a disturbing stimulus may lead to activities most of which can have no direct effect on the disturbance, although the whole sequence of them will accomplish its removal, as when the sensation of hunger leads us to cook a meal before we eat it.

These transitions are hard to understand, but it is still harder to believe that we are confronted by some radically different kind of nervous control. A purposive movement certainly appears to be guided by its effects. It is aimed at bringing the body into a fresh relation with its environment; its achievement will be signalled by a fresh pattern of afferent signals and until the pattern is achieved the exciting cause remains as a spur to any part of the motor system that can be used. In a simple affair like the flexion reflex a fresh afferent signal has arisen from without,

and movement occurs until the signals cease. In the brain fresh patterns may be formed within, by the overflow of the unstable nerve cells, without much relation to the immediate situation. They lead to activity which continues until a fresh afferent pattern reaches the brain to show that the gaze has been shifted or that the hand has closed. Purposive acts must, therefore, be moulded like the movements of walking, by the controlling afferent patterns which are set up as the act progresses. The exciting disturbance may subside owing to fatigue or distraction, anything which will deflect our purpose; but the particular afferent pattern which signals accomplishment, the temporal and spatial distribution of sensory activity, must be uniquely related to the exciting pattern which it can dissipate. It must be in some way the inverse of the exciting pattern, the key that fits that particular lock. If this argument is valid it follows that one clue to the nature of the exciting pattern is to be sought in the nature of the afferent patterns which bring it to an end.

Whether this principle can really be used as a practical guide to experiment remains to be seen. It is of no value if it cannot: it would be a waste of time, therefore, to show how it might be extended to include very complex as well as very simple high level activity, the planning of one's career as well as the shifting of one's gaze. It could be elaborated like Herbert Spencer's system of world evolution and might well meet the same fate, for if we think too far on one line we may become so enamoured of the prospect that we are unwilling to face the facts which show it to be an illusion.[1] But we can take courage from the fact that there is something very much like it in Hughlings Jackson's writings. He says: "In the lower centres there is a direct adjustment of few and simple movements to few and simple peripheral impressions. In the very highest centres (and here there is a lengthy footnote) there is an adjustment of exceedingly special movements (representing movements of the whole organism) to the most special of impressions from the environment." "Adjustment" is, of course, the key word which we have to explain or at least to amplify before we can claim any advance on Jackson's position, and electro-physiology must keep that in view if it is to have any real bearing on the working of the nervous system.

[1] It is recorded that Herbert Spencer once asked Ray Lankester to visit him as he needed some information on recent biological work bearing on evolution. Lankester had little time to give the information, for as soon as he began to mention some facts which were difficult to reconcile with the Spencerian system the strain of the interview became too great. Spencer was forced to apply the "ear-stoppers" which he carried with him to exclude fatiguing noise and the discussion was closed.

REFERENCES

ADRIAN, E. D. (1930), *Proc. Roy. Soc. B*, **106**, 596.
—— (1943), *Brain*, **66**, 289.
—— and MORUZZI, G. (1939), *J. Physiol.*, **97**, 153.
ARVANITAKI, A. (1942), *Arch. Internat. de Physiol.*, **52**, 381.
BARRON, D. A., and MATTHEWS, B. A. C. (1938), *J. Physiol.*, **92**, 276.
BREMER, F. (1940), *C. R. Soc. Biol.*, **133**, 689.
BUDDENBROOK, W. v. (1921), *Biol. Zentralbe*, **41**, 41.
DEES, V., and GRINDLEY, G C. (1947), *B. J. Psy.* To be published shortly.
ECCLES, J. C., and MALCOLM, J. L. (1946), *J. Neurophysiol.*, **9**, 139.
GRANIT, R. (1946), *J. Physiol.*, **105**, 44.
GRAY, J., and LISSMANN, H. W. (1946), *J. Exp. Biol.*, **23**, 133.
HOFFMANN, P. (1922), "Die Eigenreflexe," Berlin (Springer).
LIBET, B., and GERARD, R. W. (1938), *Amer. J. Physiol.*, **123**, 128.
LLOYD, D. C. (1943), *J. Neurophysiol.*, **6**, 317.
RENSHAW, B. (1940), *J. Neurophysiol.*, **3**, 373.
TEN CATE, J. (1940). *Arch. Néerl. de Physiol.*, **25**, 407.

PREFRONTAL LEUCOTOMY: A NEURO-ANATOMICAL REPORT.

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INTRODUCTION.

A PREVIOUS paper published by Meyer and Beck (1945) dealt with neuro-pathological problems arising out of prefrontal leucotomy. In that paper the therapeutic and psychiatric aspects were emphasized. The present paper will deal almost exclusively with neuro-anatomical investigations carried out on the same material. To ensure easy comparison, the numbering of the cases is kept identical with that in the earlier paper, which should be consulted for more comprehensive clinical and other detail. Cases 7 and 8 of the earlier paper are omitted in the present report because they were not available for more detailed study. Cases 1 and 2 are also omitted as the period of survival was too short for secondary lesions to be shown by the methods employed. They may prove suitable, however, for study of degeneration of the unmyelinated terminals by means of silver impregnation and will be included, together with other cases, in a subsequent paper. On the other hand, the histological investigation of Cases 9 and 10 has now been completed and will be included in the present report. Case 6 is not a leucotomy case, but a frontal lobectomy included on account of its valuable contribution to the present study.

There is no need to emphasize the importance of a detailed neuro-anatomical investigation of the brains of patients dying at various intervals after prefrontal leucotomy. Most of our knowledge concerning the projections to and from the prefrontal cortex has been derived from experimental observations in monkeys and apes, and there have been only a few detailed investigations of suitable human brains, to which reference will be made in subsequent sections of this paper. An operation on human beings producing a brain lesion unpredictable in precise location and extent is from a purely anatomical point of view an unqualified boon, since each case, and often each hemisphere, presents as it were a separate experiment. The leucotomy lesions of predominantly white matter cannot of course be so directly interpreted in terms of the precise cortical areas involved as can the cortical ablation lesions of animal experiments,

but analysis of a number of sufficiently varied cases should produce comparable precision.

In addition to the thalamo-prefrontal radiation, which showed some degree of degeneration in every instance, some of the cases provided an opportunity of studying the thalamic projection to the cingulate cortex, and to the premotor region; and most cases permitted observations on that portion of the frontopontile system of fibres known as Arnold's bundle. The long association fasciculi related to the prefrontal lobe have not yet been fully investigated, and are therefore only provisionally reported on in this paper. Fine fibres connecting the prefrontal cortex with the caudate nucleus, via a portion of the subcallosal bundle, have been described by several workers. Since, however, a study of the effects of leucotomy lesions on such connections calls for investigation by means of silver impregnation, we have deferred treatment of the problem. Likewise the centre-median nucleus, whose still obscure fibre connections are under investigation, will be the subject of a separate paper.

As regards the prefrontal cortex rostral to the lesion it is not yet possible to say whether the slight cellular loss in the third layer noted in some of the cases is due to the leucotomy or to other causes. Extensive control counts of normal and other cases are necessary, and these are not yet completed.

Case Material and Description of the Primary (Surgical) Lesions.

Where the primary lesions in the two hemispheres were in position and extent practically identical, and hence the secondary changes presumably symmetrical, only one side was studied in detail. In all, eight hemispheres were investigated.

The extent of the lesion was in each case determined by means of coronal sections stained by cresyl violet for cells, and Heidenhain's modified iron hæmatoxylin method for myelin. The diagrams of the primary lesions are made from such sections. Cross-hatching indicates complete loss of tissue; single-hatching represents incomplete loss with nerve-cell or fibre damage.

Numerical cortical areas referred to in the text and indicated in the diagrams are those of Brodmann.

Case 3 was a 72-year-old man, suffering from acute agitated depression of four years' duration, who did not improve after prefrontal leucotomy (Watts' technique), and who died two months after the operation from uræmia due to hypertrophy of the prostate.

The brain showed slight general atrophy, and a small lesion in the middle of the inferior frontal convolution on either side indicated the site of entry of the leucotome.

The *Left Hemisphere* contained a cystic softening greatest in extent in the plane half a centimetre posterior to the tip of the anterior horn of the lateral ventricle. At this level (fig. 1B) the lesion involved the deep white matter of the inferior and middle frontal gyri (areas 45 and 46), parts of the cortex in the depths of the horizontal ramus of the lateral fissure, and the white matter of the most lateral gyrus of the orbital region (area 47). The ependyma of the anterior horn was ruptured. Rostrally the lesion extended for just over half a centimetre, spreading dorsally to end in the deep white matter of areas 9 and 8 (fig. 1A). Caudally it extended for one centimetre, involving the wall of the ventricle for half that distance, and gradually ended in the deep central white matter. At no point was there damage to the white matter or cortex of the middle and medial orbital region (areas 11 and 12), or of the cingulate gyrus (area 24). The right hemisphere exhibited a lesion very similar in position and extent.

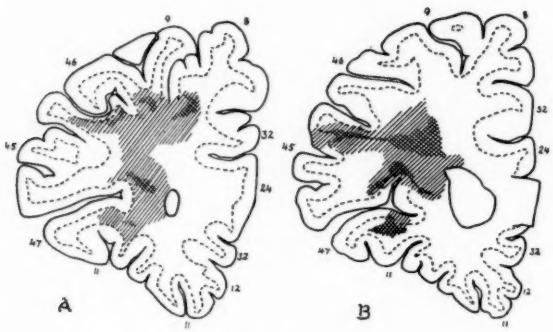

FIG. 1.

Case 4 was a woman with paraphrenia of two years' duration, who died at the age of 50, four months after prefrontal leucotomy (Watts' technique). After the operation her hallucinations disappeared but she developed a severe frontal-lobe deficit syndrome with marked restlessness. Her death was due to exhaustion resulting in thiamine deficiency. The uncut brain displayed no evidence of the leucotome incisions.

The *Left Hemisphere* in the plane of the tip of the anterior horn of the lateral ventricle revealed a large area (fig. 3A) of cystic hæmorrhagic softening, maximum at that level, occupying the whole of the deep white matter of the superior, middle, and inferior frontal gyri (areas 6, 8, 9, 46 and 45). Parts of the cortex in the depths of the superior frontal sulcus and the horizontal ramus of the lateral fissure were also affected. On the medial surface the cortex of the cingulate gyrus (area 24) was damaged and the deep white matter of area 32 affected. The lesion dwindled out half a centimetre rostrally in the white matter of the middle frontal gyrus. One centimetre caudally (fig. 3B) it divided into a ventral patch of softening breaking into the lateral ventricle and involving the insula, claustrum and dorso-lateral aspects of the putamen, internal capsule and caudate nucleus; and a dorsal slit-like cyst occupying the depths of the white matter corresponding to areas 8

and 9. Both of these lesions terminated three millimetres further caudally. At no point was the orbital region (areas 47, 11 and 12) involved.

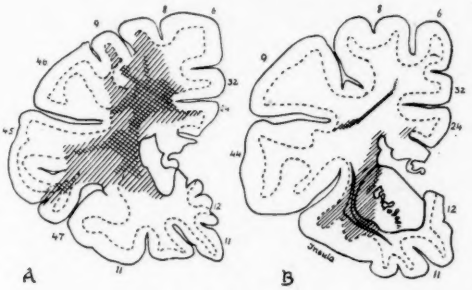

FIG. 3.

The *Right Hemisphere* displayed a lesion less extensive than on the left, and centred one centimetre more posteriorly. At that level (fig. 5B) it involved the cortex in the superior frontal sulcus (area 8), and the deep white matter of areas 8, 6, 32 and 24. Then, penetrating the lateral ventricle, it damaged the most dorsal parts of the caudate nucleus, putamen, internal capsule and claustrum. Three

FIG. 5.

millimetres caudally the lesion dwindled out in the white matter of area 6. One centimetre rostrally (fig. 5A) the softening involved a small part of the deep white matter of the superior frontal gyrus (areas 6 and 8), cortex and white matter of the inferior frontal gyrus (area 44), and the periventricular white matter dorsal to the caudate nucleus. Two millimetres further rostrally it petered out in the periventricular white matter. At no point in this hemisphere were the cingulate gyrus or the orbital region affected.

Case 5 was a man with violent and destructive schizophrenia of twenty years' duration who died in status epilepticus at the age of 44, seventeen months after prefrontal leucotomy (Watts' technique) which had not modified his psychosis.

The brain exhibited a small puncture hole just above the anterior end of the Sylvian fissure on either side. Coronal sections showed that the leucotomy cuts had been made about one and a half centimetres in front of the genu of the corpus callosum.

The *Left Hemisphere* at the level of the leucotomy cut (fig. 7A) showed an old hæmorrhagic cystic softening destroying the cortex of the medial surface extensively in the region of areas 32 and medial 9, and the cortex of the convexity slightly in the middle frontal convolution (area 10); and involving the white matter of these

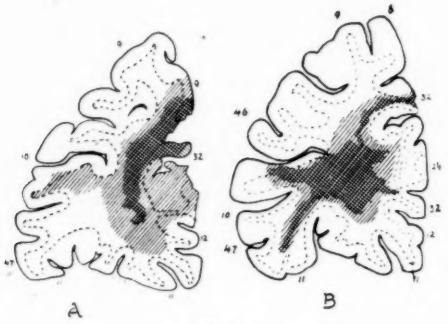

FIG. 7.

and the medial orbital region (areas 12 and medial 11). Rostrally the lesion extended for one centimetre, ending in the white matter of area 32. One centimetre caudally (fig. 7B) it involved the white matter of the inferior frontal and lateral orbital gyri (area 47 and lateral 11) severely, and the cingulate white matter (area 24) slightly. It terminated in the orbital white matter about half a centimetre posterior to the level of the rostral tip of the genu of the corpus callosum. At no point was the dorsal half of the prefrontal lobe (areas 46 and lateral 8 and 9) involved.

The *Right Hemisphere* contained a lesion maximal in the same plane as on the left, but more extensive, occupying almost the whole of the white matter corresponding to areas 32, 9, 10, 47, 11 and 12, and involving the cortex of areas 32, 9

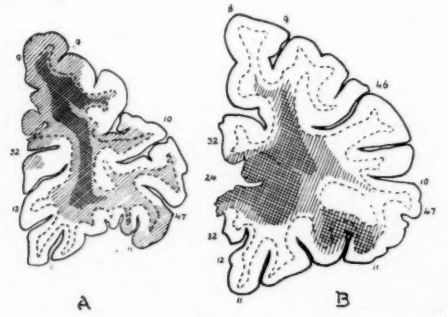

FIG. 9.

and 47 (fig. 9A). One and a half centimetres rostrally the lesion petered out in small cysts in the white matter of the superior frontal gyrus and medial orbital region. One centimetre caudally (fig. 9B) it involved the cortex of the cingulate

gyrus (area 24). Half a centimetre further caudally it spread into the genu of the corpus callosum. The main lesion terminated in the central white matter at a level one centimetre posterior to the tip of the genu, while the corpus callosum softening dwindled to extinction about two centimetres still more posteriorly. Apart from the surgical lesions the cerebral cortex manifested no abnormality beyond occasional small patches of recent softening, particularly near the precentral region. These were probably caused by anoxia during the epileptic convulsions.

Case 6 was a woman who died at the age of 60, six weeks after a right frontal lobectomy aimed at removal of a basal meningioma causing bilateral optic atrophy. She recovered from the primary operation but one month later, after the second-stage operation, lapsed into a condition of pathological sleep which persisted until her death.

Autopsy examination of the right frontal lobe showed that it had been amputated at the level of the genu of the corpus callosum (through areas 8, 9, 46, 45, 47, 11, 12, 32 and 24). A well-encapsulated tumour-mass involved the optic chiasma and hypothalamus reaching posteriorly to the level of the mamillary body. The striate body and anterior parts of the globus pallidus had been displaced dorsally. There was recent softening in the right side of the corpus callosum to a caudal depth of one centimetre, and in both areas 24 and 23 of gyrus cinguli.

The left hemisphere and the midbrain and pons were not available for examination.

Case 9 was a man with schizophrenia of three years' duration who died of pulmonary tuberculosis at the age of 39, two years after prefrontal leucotomy (Crombie's technique) which resulted in disappearance of his hallucinations, delusions and suicidal depression.

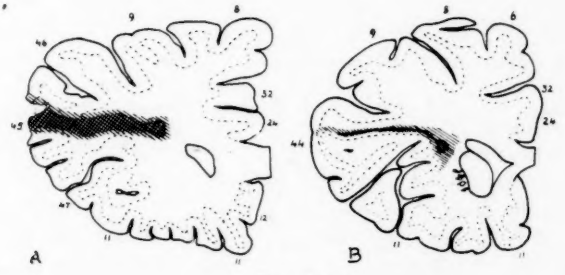

FIG. 12.

The brain showed a small leucotome mark in the triangular portion of the operculum on either side. Coronal sections revealed the greatest extent of the lesion to lie, on both sides, at the level of the genu of the corpus callosum.

The *Right Hemisphere* at this level (fig. 12A) contained a slit-like smooth-walled cyst stretching transversely in the inferior frontal gyrus (area 45) from the cortex to within a centimetre of the dorsal angle of the anterior horn of the ventricle. Narrowing gradually, it extended in the same horizontal plane rostrally for one and a half centimetres (into area 46), and caudally (fig. 12B) for one centimetre (into area 44). The left hemisphere lesion was almost identical in position and extent.

Case 10 was a woman of psychopathic personality afflicted with gross hysterical outbursts since childhood, who died at the age of 28 three years after prefrontal leucotomy (Crombie's technique) which had rendered her outbursts much milder and less frequent. Two and a half years after the operation she developed persistent joint pains, skin ulcers and streptococcal stomatitis, and six months later died of broncho-pneumonia.

The brain displayed no external evidence of the leucotomy incisions.

The *Left Hemisphere* contained (fig. 14A) an area of cystic softening and demyelination maximum at a level half a centimetre posterior to the anterior tip of the genu of the corpus callosum. At this level it stretched transversely through

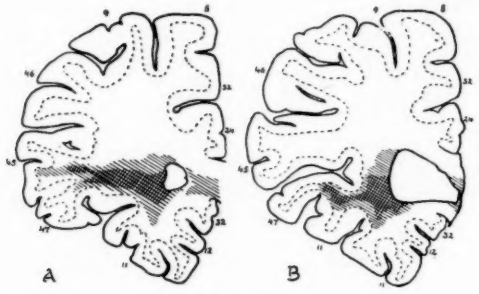

FIG. 14.

the white matter of the inferior frontal gyrus (area 45) from just under the cortex to the border of the anterior horn of the ventricle. Half a centimetre rostrally it petered out just lateral to the ventricle. Caudally it passed through the cortex in the depths of the horizontal ramus of the lateral fissure to run into (fig. 14B) the white matter of the gyri of the lateral orbital region (areas 47 and lateral 11). It terminated in the deep white matter just at the anterior tip of the striate body. Coextensive with the white matter lesion there was demyelination and gliosis in the corpus callosum stretching across the midline from the medial side of the ventricle, as if the leucotome had injured it after piercing the ventricle. The right hemisphere exhibited a very similar lesion.

DESCRIPTION AND DISCUSSION OF THE SECONDARY LESIONS.

Where both hemispheres of a case were investigated the side under discussion will be indicated in brackets.

In each hemisphere studied serial coronal sections were made of the thalamus in an antero-posterior direction. From celloidin blocks twenty sections cut at 20μ thickness were alternated with five sections at 30μ. Every fiftieth section was stained for nerve cells and glial nuclei (Cresyl Violet), every fifty-first section for myelin sheaths (Heidenhain), and every hundredth section for glial fibres (Holzer). In Cases 4 (Right), 5 (Right) and 9 the series was extended rostrally to the anterior pole of the striate body, and in 5 (Right), 9 and 10 caudally into the pons.

The Projection of the Anterior Nucleus of the Thalamus.

Cases 4 (Left and Right), 5 (Left and Right), and 6 show retrograde degeneration within the anterior nuclear group.[1] The remaining cases are negative in this respect.

Case 4 (*Left*) contains a region of heavy gliosis within the lateral half of nucleus anteromedialis (figs. 4 and 17), stretching through 150 sections. Few nerve cells remain in the region, and those which do so are shrunken and deeply stained. Holzer staining shows astrocytic proliferation in the affected part.

Case 4 (*Right*) displays (fig. 6) retrograde changes similar to those in Case 4 (Left) but slightly less extensive.

Case 5 (*Left*) shows a region of gliosis and reduction in nerve cells in the ventral part of nucleus anteromedialis (fig. 8), stretching through 200 sections. The cells remaining in the affected region contain an eccentric nucleus and yellowish vacuolic cytoplasm. This type of cell change is, however, encountered in intact parts of the nucleus and is obviously due to increase of lipofuscin.

Case 5 (*Right*) exhibits (fig. 10) the same features in nucleus anteromedialis as described in 5 (Left).

Case 6 shows less advanced gliosis and rather pale staining of many nerve cells throughout the whole anterior group, but more marked in the anteromedial than in the anteroventral nucleus (fig. 11). Under high magnification the nerve cells throughout both are seen to be undergoing typical retrograde degeneration.

Discussion.

It has been established by Le Gros Clark (1932) and Le Gros Clark and Boggon (1933) in rats and cats respectively that elements of the anterior nuclear group of the thalamus are related by corticopetal fibres with the whole length of gyrus cingularis. This has been confirmed and elaborated by Walker (1938*a*) in chimpanzees and Lashley (1941) in rats, both of whom find evidence indicating that nucleus anteromedialis projects to the rostral part of the cingulate gyrus, nucleus anteroventralis to the caudal part. Observations pointing to a similar system of projection in man have been made by Le Gros Clark and Russell (1940) in a case of diffuse porencephaly and sclerosis of one hemisphere, by Freeman and Watts (1942) in preliminary anatomical studies of leucotomized brains, and by Norman (1945) in a case of bilateral frontal atrophy.

Our cases confirm these human observations. Thus in Cases 4 (Left and Right) and 5 (Left and Right), in which only the rostral portion of the cingulate gyrus was involved in the primary lesion, only nucleus anteromedialis shows degenerative changes, whereas in Case 6 in which postoperative softening involved almost the whole length of the cingulate gyrus, there is in addition degeneration in nucleus anteroventralis. Our findings therefore do not support the suggestion derived from oscillo-

[1] We distinguish nucleus anteromedialis from nucleus anteroventralis not in virtue of any cytoarchitectural differences but simply in accordance with the topographical description of Sheps (1945).

graphic studies on monkeys and chimpanzees (Bailey, von Bonin, Davis, Garol, McCulloch, Roseman and Silveira, 1944) that in primates there is no thalamic projection to the anterior cingulate gyrus.

Walker (1938) and Freeman and Watts (1942) have suggested that nucleus anteromedialis projects also to the orbital surface of the frontal lobe. Likewise Von Bonin (1945) does not exclude the possibility that one of the anterior thalamic nuclei may project to area 47 (whose cytoarchitecture he finds to resemble that of area 24). We cannot entirely rule out this possibility since there was no instance among our cases of a primary lesion in the orbital region unaccompanied by damage to the cingulate gyrus. On the other hand, the consistent correlation within our eight hemispheres between primary lesion in the cingulate gyrus and secondary lesion in the anteromedial nucleus does tend to render such an additional orbital projection improbable.

Le Gros Clark and Boggon (1933) in cats, and Lashley (1941) in rats, have described a definite spacial correlation of fibres: a dorsolateral-ventromedial axis in the anterior nucleus projecting to a caudal-cephalic axis of the cortical field. Our cases demonstrate that to some extent at least this holds good for man. Thus Cases 5 (Left and Right), in which only the anterior tip of the cingulate gyrus was affected in the primary lesion, resulted in retrograde degeneration involving the medial half of nucleus anteromedialis, whereas Cases 4 (Left and Right) where the cingulate lesion was more caudal (though still within area 24) produced degeneration within the lateral half of nucleus anteromedialis.

The thalamo-cingulate fibre tract will be discussed in a later section.

THE PROJECTION OF THE DORSO-MEDIAL NUCLEUS OF THE THALAMUS.[1]

All eight hemispheres show retrograde degeneration of greater or lesser degree in this nucleus; all in the parvicellular part, and three also in the magnocellular part.

[1] In monkeys Walker (1940) describes the most lateral portion of this nucleus as a distinct "paralamellar" part composed of larger well-staining cells within the internal medullary lamina. Le Gros Clark and Boggon (1935) make no such distinction in the Macaque thalamus; Sheps (1945) in his description of normal human thalamic nuclei makes no such sub-division; and we have found such a discrete cell region very inconstant in human material. We include it therefore, when it occurs, in our "dorsolateral" and "ventrolateral" portions of pars parvicellularis. We distinguish, for descriptive and correlation purposes, additional "central" and "medial" portions of pars parvicellularis.

Case 3.—The magnocellular part of the nucleus is intact throughout. The parvicellular part (fig. 2) shows, at the rostral tip of the nucleus, cell poverty and gliosis in its ventrolateral region. 50 sections more posteriorly the degeneration spreads to involve in addition the dorsolateral region. 100 sections more caudally it shifts centrally and involves the central and medial regions until 300 sections still more caudally it peters out at the level of the junction of the rostral and middle thirds of the centromedian nucleus. Some of the surviving nerve cells within the

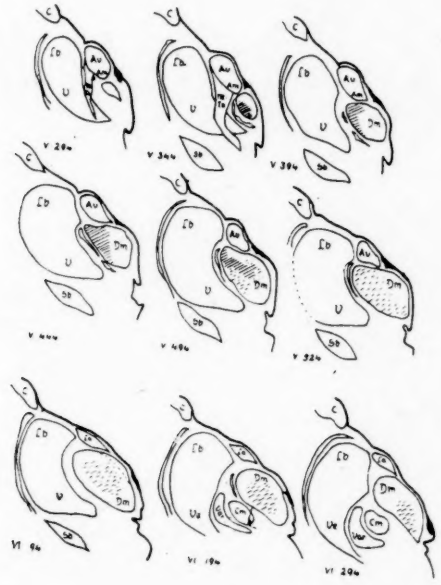

FIG. 2.

affected regions show retrograde degeneration; in others there is only shrinkage with nuclear pyknosis. Holzer preparations reveal marked astrocytosis throughout the parvicellular part, densest in the region described above as degenerated. The magnocellular part is free of such proliferation.

Case 4 (*Left*).—The magnocellular part is intact. The parvicellular part (fig. 4) shows cell loss and glial proliferation at the rostral tip of the nucleus in its lateral region. 50 sections caudally the degeneration spreads to involve all but the medial region. For the next 100 sections the lesion is most severe in the lateral half, and then for 200 sections in the central region. Thereafter it spreads ventrally

before terminating 100 sections further caudally at the level of the middle of the centromedian nucleus. Even in the most gliosed parts there are still a number of nerve cells. Some of these show an eccentric nucleus and partial reduction in tigroid substance; others exhibit simple atrophy with pyknosis of the nucleus. Many

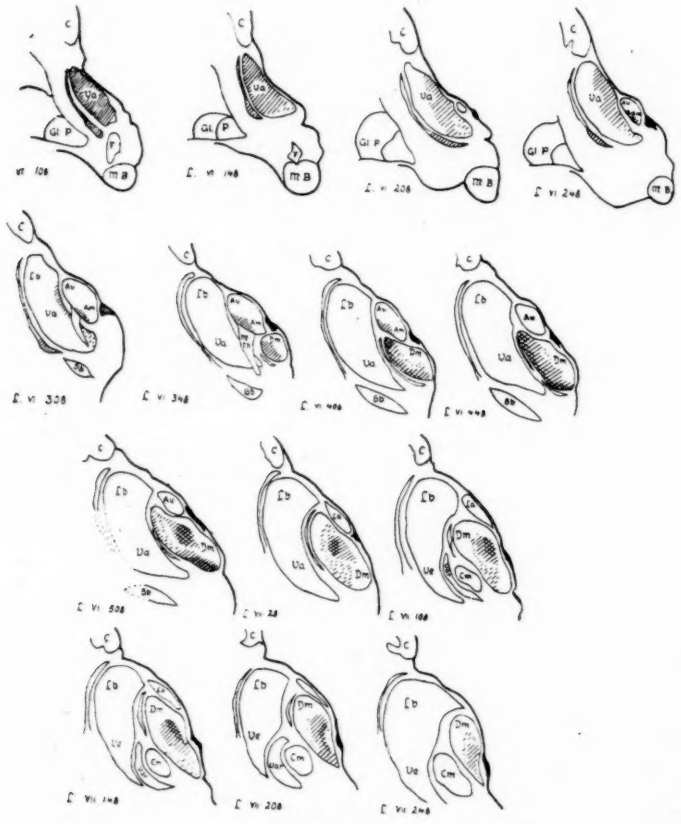

FIG. 4.

contain excess of lipofuscin. The macroglia is strongly proliferated with activated nuclei and visible cytoplasm, and often forms "gliarasen." There is also a slight mesodermal and microglial proliferation. In Holzer preparations a marked astrocytosis is seen in the degenerated regions.

Case 4 (*Right*).—The dorsomedial nucleus on this side shows degeneration of nerve cells and glial proliferation in the parvicellular part (fig. 6) similar in distribution to that described on the left side, except that the severe degeneration commences and terminates at levels about 50 sections more posteriorly.

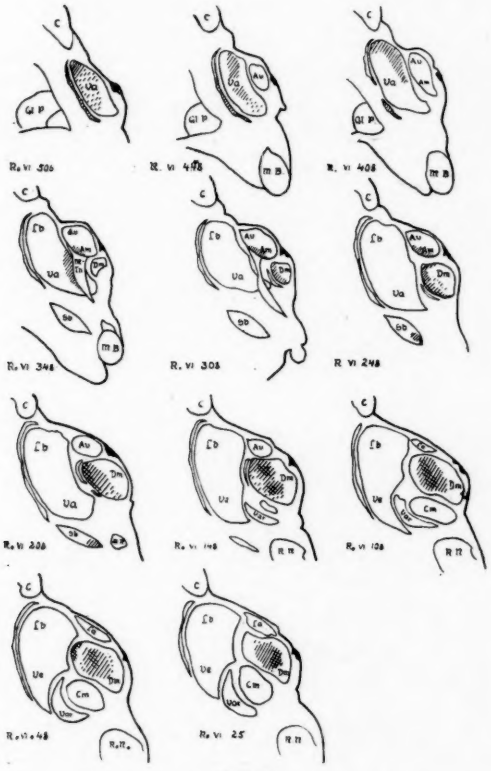

FIG. 6.

Case 5 (*Left*).—The magnocellular part (fig. 8) shows severe cell loss and glial proliferation from a level 100 sections behind the rostral tip of the dorsomedial nucleus to the level of the anterior tip of the centromedian nucleus. The parvicellular part is at the rostral tip of the nucleus cell-poor and gliosed throughout. 50 sections more caudally the severest degeneration lies in the central and medial portions, and remains in that location until the lesion terminates 200 sections farther caudally at the level of the junction of the anterior and middle thirds of

the centromedian nucleus. Posterior to this cresyl violet preparations reveal no abnormality, but Holzer staining shows some glial reaction. Many of the remaining nerve cells in the degenerated regions of both the magno- and the parvicellular

FIG. 8.

parts display shrunken cytoplasm and a pyknotic nucleus but no typical retrograde degeneration.

Case 5 (*Right*).—The magnocellular part (figs. 10 and 18) exhibits degenerative changes almost identical with those on the left. The parvicellular part displays

the same changes as in the left nucleus, except that the severest degeneration remains slightly more dorsal, and degeneration extends for 50 sections more caudally.

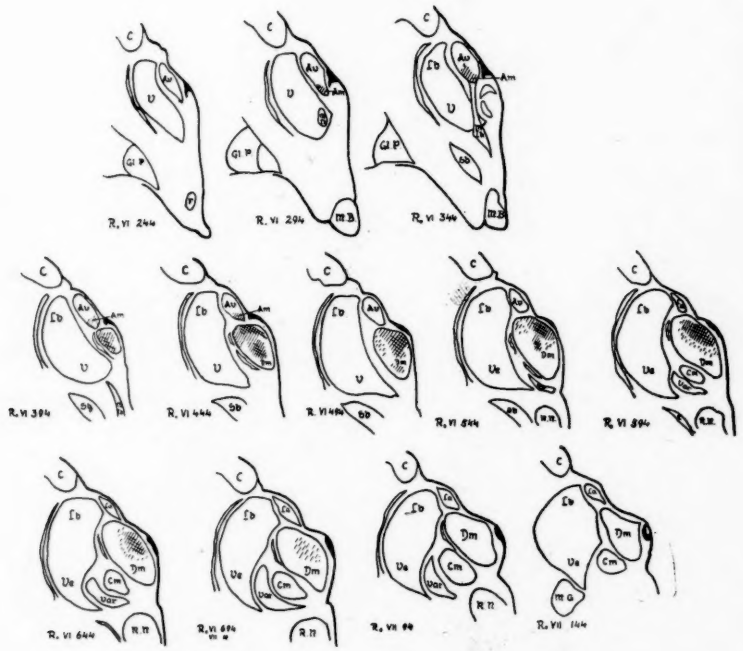

FIG. 10.

Case 6.—The magnocellular part (fig. 11) is, except for a small dorsal cap at the rostral tip of the nucleus, indistinguishable due to severe degenerative changes. The parvicellular part is very cell-poor throughout from the anterior tip of the nucleus to the level of the junction of middle and posterior thirds of the centromedian nucleus, and slightly degenerated for 100 sections more posteriorly. The

degeneration is at all levels severest in the medial half. In the affected regions all the remaining nerve cells show retrograde degeneration. Holzer staining reveals marked astrocytic proliferation, especially in the medial half of the region.

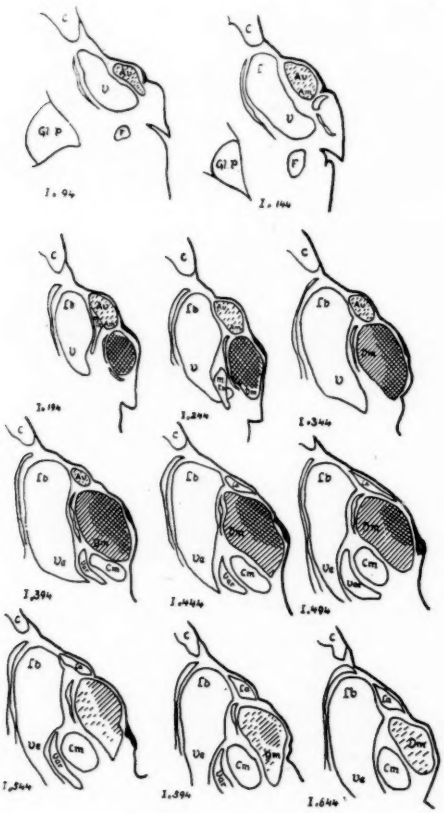

FIG. 11.

Case 9.—The magnocellular part appears normal. The parvicellular part (fig. 13) shows slight cell loss and gliosis at the rostral tip of the nucleus in its dorsolateral region. This degeneration extends caudally for only 150 sections. Remaining nerve cells in the affected region are slightly shrunken with pyknotic nucleus.

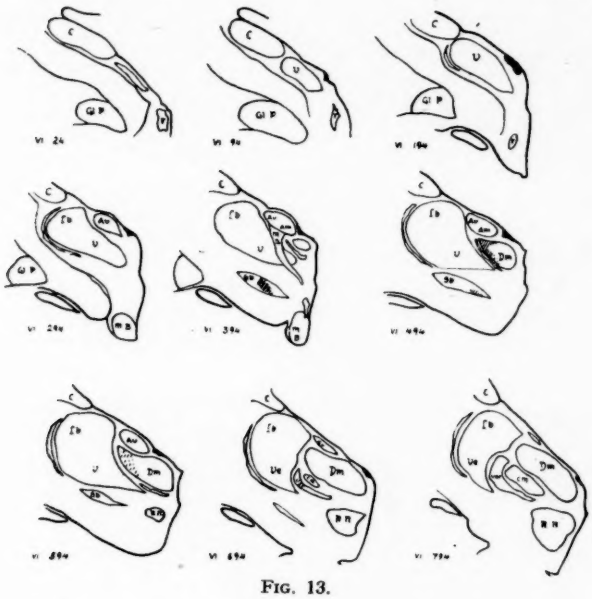

FIG. 13.

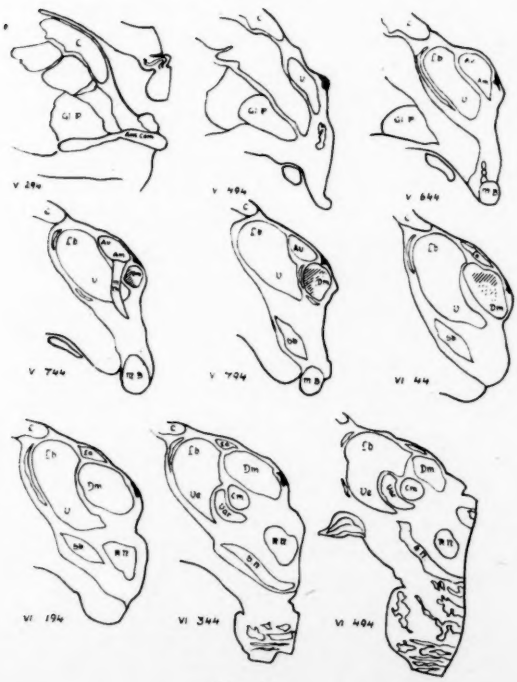

FIG. 15.

Case 10.—The magnocellular part is unaffected. The parvicellular part (fig. 15) shows marked cell loss and gliosis at the rostral tip of the nucleus in its lateral region. 50 sections more caudally the degeneration spreads into the dorsolateral region. Then through 200 sections it moves dorsocentrally before petering out in the medial portion 150 sections still more posteriorly. Holzer staining reveals mild astrocytic proliferation in these regions.

Discussion.

Walker (1938) came to the conclusion that, in monkeys, roughly a dorsoventral axis of the prefrontal lobe corresponds to a latero-medial axis of the dorsomedial nucleus. This axial principle was previously adopted by two of us (Meyer and Beck, 1945); but the more detailed analysis of the lesions is now as follows:—

The dorsolateral portion of pars parvicellularis is degenerated in Cases 3, 4 (Left and Right), 6, 9 and 10. In Case 9 it is the only region affected. It is intact in Case 5 (Left and Right). These facts, when correlated with the primary lesions, suggest that this portion projects to, roughly, the inferior frontal gyrus in areas 45 and 46 (i.e. to the neighbourhood of the usual site of leucotome entry). The ventrolateral portion of pars parvicellularis shows degeneration in Cases 3, 4 (Left and Right) and 6. The only affected area in the primary lesions common to these four cases (and not involved in cases not showing such retrograde degeneration) is area 8 in the superior frontal gyrus. The central portion of pars parvicellularis is degenerated materially in all except Cases 9 and 10. Its involvement would appear therefore to correlate best with a primary lesion to the middle frontal gyrus in areas 46 and 9 (or 10). The medial portion of pars parvicellularis show degeneration in Cases 3, 5 (Left and Right), 6 and 10. It therefore apparently projects to the lateral part of the orbital region (areas 47 and lateral 11). Pars magnocellularis exhibits retrograde degeneration in only Cases 5 (Left and Right) and 6. Since these are the only three hemispheres in which the primary lesion involved the medial half of the orbital region, this might indicate that this most medial portion of the dorsomedial nucleus projects to areas 12 and medial 11.

It is evident that many of these observations correspond with Walker's findings in monkeys—for instance the projection of pars magnocellularis to the orbital cortex, and of the central portion of pars parvicellularis (Walker's midportion) to the cortex of the dorsal convexity. On the other hand, projection of the dorsolateral portion of pars parvicellularis (Walker's superior paralamellar portion) to area 45, and of the ventrolateral portion (Walker's inferior paralamellar portion) to area 8, is the exact reverse of

Walker's findings in monkeys. Again, association of pars magnocellularis with only the medial half of the orbital cortex is a more limited distribution, apparently, than in monkeys. We include area 12 in this medial orbital projection of pars magnocellularis, in contradistinction to Walker's finding that area 12 in monkeys receives fibres from the ventral part of the dorsomedial nucleus. We are in agreement, however, with his conclusion that area 10 receives no appreciable projection from the dorsomedial nucleus (cf. our observations on the prefronto-pontile tract). With regard to McCulloch's (1946) contention that area 47 receives no dorsomedial radiation in monkeys it is interesting to note that in Case 3 in which area 47 was the only part of the orbital region involved in the primary lesion there is retrograde degeneration in the medial portion of pars parvicellularis.

It should be remembered that our observations are derived from lesions of the white matter and cannot therefore be as accurate as those obtained from animal experiments by ablation of cortical areas. Further correlations in a larger number of human cases are clearly needed to clarify and validify these points of difference, to determine whether a simple monaxial correlation between nucleus and cortex can be maintained in man, and to decide whether in fact the organization of the projection of the dorsomedial nucleus in man reveals any fundamental deviation from its plan of organization in monkeys and apes.

Walker (1938) has demonstrated that in the macaque anterior parts of the dorsomedial nucleus project to cortical areas slightly more anteriorly than do posterior parts of the nucleus. Such an anteroposterior axial relationship is shown by our human cases. Thus in Cases 5 (Left and Right), where the primary lesion was essentially anterior to the tip of the corpus callosum, the secondary lesion in the dorso-medial nucleus extends only so far as the level of the junction of the anterior and middle thirds of the centromedian nucleus; whereas in Cases 4 (Left and Right), in which the primary lesion was essentially caudal to the tip of the corpus callosum, the secondary lesion extends to the level of the middle of the centromedian nucleus. Again, in Case 4 (Right) in which the primary lesion was 1 cm. posterior to that of Case 4 (Left), the secondary lesion extends 50 sections more posteriorly in the dorsomedial nucleus in man.

Walker (1938) has further suggested that an anteroposterior lamellar plane in the dorsomedial nucleus may project to each point in the cortex. Our cases so far produce no clear evidence on this point, though the fact that, for instance, the secondary lesion always involves the anterior (dorsolateral) tip of the nucleus, no matter how remote the primary lesion from

the anterior pole of the frontal lobe, indicates that some such system may well pertain.

The existence of a cortical projection arising from the magnocellular half of the dorsomedial nucleus has been definitely established by Walker (1940) in monkeys, Le Gros Clark and Russell (1940) in a human case of complete cortical atrophy, Meyer and Beck (1945), and Norman (1945) in a human case of frontal lobe atrophy. Walker (1940) has shown that in monkeys the projection is to the orbital region. Our cases, as described above, point to a like projection in man, but confined to the medial half of the orbital region. It is not possible to be certain of the significance of the small anterodorsal cap of cells which remains intact even in the lobectomy case (Case 6). It may represent cells which project periventricularly, and so accord with Walker's (1936) observation in monkeys that magnocellular cells degenerate after certain lesions in the hypothalamus. Another possibility is that these cells simply project to posterior parts of the orbital region not damaged by the surgical lesion, for Le Gros Clark and Russell (1940) and Norman (1945) found no remaining trace of the magnocellular nucleus in their cases of cortical atrophy.

However that may be, the existence of a magnocellulo-orbital projection is unequivocal, and is probably of great functional significance in view of the established projection of hypothalamic nuclei to pars magnocellularis (Roussy and Mosinger, 1933). It opens up the probability of a relatively direct hypothalamo-prefrontal connection, and so provides an anatomical pathway to account for the electrical effects in medial orbital areas found on vagal stimulation in cats (Bailey and Bremer, 1938) and contributes to the neural mechanism by which emotionally induced autonomic changes have recently been demonstrated to produce effects on the cerebral circulation and rhythm (Darrow, Green, Davis and Garol, 1944).

PROJECTION OF THE SUBMEDIAL NUCLEUS OF THE THALAMUS.

This nucleus shows degenerative changes in four of the cases.

Case 3 in cresyl violet sections shows cell poverty without gliosis in nucleus submedius, and in Holzer preparations dense glial proliferation in that region. The nerve cells remaining exhibit mild retrograde degeneration.

Case 4 (*Left*) in cresyl violet sections displays slight cell poverty in nucleus submedius, and glial proliferation in both submedius and centralis medialis. Holzer preparations reveal astrocytic proliferation in both nuclei. Their remaining nerve cells show shrinkage and increase of pigment.

Case 4 (*Right*) exhibits changes similar to those on the Left, but slightly less pronounced.

Case 6 shows both vacuolic pigmentary degeneration and retrograde degeneration in the nerve cells of the submedial nucleus in cresyl violet sections, and macroglial proliferation in the corresponding regions in Holzer preparations.

Discussion.

Walker (1938) finds no degeneration in nucleus submedius in monkeys after hemidecortication. Our cases therefore seem to indicate that this intralamellar nucleus has acquired a new direct or indirect cortical projection in man. The only mention of a cortical connection for nucleus submedius which we have been able to find in the literature is by Sheps (1945) who found this nucleus partially degenerated in two human cases, one of generalized cortical atrophy, the other of a large cystic lesion in the frontal convexity. Pars parvicellularis of the dorsomedial nucleus was severely degenerated in both of his cases.

A noteworthy feature of our four cases is that they are also the only four cases which show a degeneration in the ventrolateral region of pars parvicellularis of the dorsomedial nucleus. It would appear, therefore, that in man these two adjacent nuclear masses are closely related in their cortical projection (which may be area 8 of the superior frontal gyrus, according to our correlations discussed in the preceding section), either through separate pathways or through intrathalamic synaptic connections. This parallel degeneration of adjacent but distinct nuclei is reminiscent of the degeneration of the reticular *vis-à-vis* the ventral nucleus referred to in the next section.

Projection of the Anterior Ventral and the Reticular Nuclei of the Thalamus.[1]

Only Case 4 (Left and Right) exhibits degenerative changes in these nuclei.

Case 4 (*Left*) shows (fig. 4) reduction in nerve cells and dense gliosis in the most anterior tip of ventralis anterolateralis and anteromedialis (i.e. of nucleus Ventralis Anterior). Farther caudally the degeneration becomes more intense and moves medially until at the level of the rostral tip of the anterior nuclear complex the whole medial half of the ventral nucleus is very heavily gliosed and almost devoid of nerve cells. The few cells which do remain are slightly shrunken with vacuolic cytoplasm. More posteriorly the area of degeneration dwindles in the medial-most part of lateralis "b" and ventralis anteromedialis (i.e. of nucleus Ventralis Lateralis), and finally peters out against the internal medullary lamina at the level of the rostral tip of the dorsomedial nucleus. Holzer staining reveals considerable astrocytic proliferation mixed with the proliferated microglial cells throughout the affected area. It will be shown in the next section that a portion

[1] The differences between British and American subdivision and nomenclature of the ventral and lateral nuclei of the thalamus at their rostral ends are not simple to reconcile. For the purposes of this paper the terminology of Le Gros Clark will be followed and the corresponding nomenclature of Walker added in brackets.

of the gliosis described here is related to degeneration in fibres of passage from the dorsomedial nucleus into the internal capsule.

The reticular nucleus shows cell poverty and gliotic changes which anteriorly, adjacent to the degeneration in the ventral nucleus, involve the full dorsoventral extent of the nucleus, but posteriorly become gradually more limited to the ventromedial portion, and finally terminate in its most ventral tip at the same level as the degeneration in the ventral nucleus disappears.

Case 4 (*Right*) exhibits (fig. 6) almost identical changes in its ventral and reticular nuclei.

Discussion.

Le Gros Clark and Boggon (1935; Case L) in a macaque found degeneration in the medial portion of ventralis anteromedialis and the neighbouring part of lateralis "b" after a cortical lesion confined to area 6. Stern (1941) found heavy degeneration in the anteromedial part of both ventrolateral nuclei in a human case of traumatic injury which had involved the premotor area in both hemispheres. Our Case 4 (Left and Right) confirms this relationship of ventralis anteromedialis to area 6 in man, since it is the only case in which there is primary damage to area 6, and which shows retrograde degeneration in ventralis anteromedialis. It seems no longer necessary to consider the possibility that the degeneration in the ventral nucleus might be attributable to the bilateral damage to the striate body in this case, for Sheps (1945) has demonstrated that the entire anterior ventral nucleus degenerates in man after extensive cortical destruction and hence, by implication, that it has lost its projection to the striatum postulated in monkeys (Walker, 1938).

Our negative findings in the ventral nucleus in Cases 3 and 6 where area 8 (but not area 6) was involved in the primary lesion do not accord with conclusions reached by Norman (1945). He found gross degeneration in the medial third of ventralis lateralis on both sides in a case of atrophy of both frontal lobes exclusive of the precentral gyri, and considered that the cortex responsible lay anterior to area 6. It would seem possible, from his illustrations, that cavitation into the white matter of area 6 may have been responsible for the nuclear lesions.

The post-operative restlessness in our case may have been due either to the involvement of area 6 or to the damage to the striate body. Shenkin and Ruch (1943) find that stimulation of the posterior region of area 11 (area 13 of Walker) in the macaque produces restlessness, but this region was not affected in either side of Case 4.

Degeneration in the reticular nucleus was found by Walker (1938) contiguous to retrograde cell changes in adjoining nuclei. He concludes that this nucleus therefore projects to the same cortical area as its adjacent

nuclei. Our two cases seem to conform with this principle. What has been said about the submedial nucleus and the adjacent portion of the dorsomedial nucleus also applies here.

Note on the Pathway of the Anterior Thalamic Radiation.

All the cases show in cresyl violet stained sections a large gliosed patch in the internal capsule ventral to the caudate nucleus at a level just anterior to the thalamus (fig. 16D).

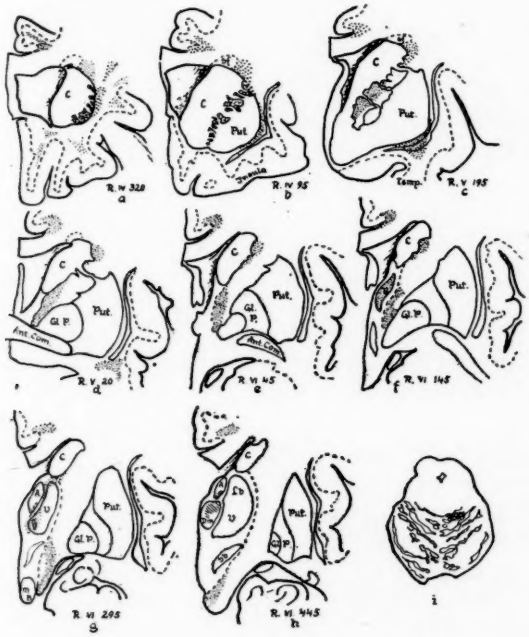

FIG. 16.

On following this gliosis through more posterior sections the whole of it in Case 3, and a portion of it in the rest of the cases, is seen to diverge medially (figs. 16F and 19) and pass through the dorsomedial half of nucleus ventralis anteromedialis (i.e. of Ventralis Anterior) until at, or just before, the level of the anterior border of the mamillo-thalamic tract it crosses the internal medullary lamina into the anterior extremity of the dorsomedial nucleus (figs. 16G, H). Traced through the more anterior sections available in Case 4 (Right) the whole gliosed patch gradually shifts dorsally in the anterior limb of the internal capsule until at levels anterior to the globus pallidus it occupies the upper half of the capsule. In Case 5 (Right) the whole of the internal capsule remains gliosed to its most anterior extremity (figs. 16B, A).

An additional smaller separate patch of gliosis can be seen in Cases 4 (Left and Right) and 5 (Left and Right). Followed posteriorly it remains at the lateral border of the subcallosal fasciculus for a considerable distance (figs. 16A, B, C). Then, becoming less discrete, at least part of it moves down the internal capsule in the path of, and dorsal to, the main patch in such a way that as the latter passes into the dorsomedial nucleus, it enters the dorsal edge of ventralis anteromedialis (fig. 16C). It traverses the dorsomedial border of this nucleus and then, passing into and down the internal medullary lamina, terminates in the ventrolateral angle of the anteromedial nucleus (fig. 16H).

Heidenhain preparations reveal an appreciable demyelination throughout the intracapsular course of these patches.

Discussion.

There can be little doubt that the portion of the larger gliosed patch described above represents the course of (degenerated) fibres projecting from nerve cells in the dorsomedial nucleus to the prefrontal cortex. Its shift dorsally in the internal capsule in the more anterior sections of Case 4 (Right) indicates the path taken by fibres of parvicellular origin radiating towards the cortex of the convexity. The additional ventral gliosis in anterior sections of the internal capsule of Case 5 (Right) indicates the path taken by fibres of magnocellular and medial parvicellular origin radiating towards the orbital cortex.

It seems equally evident that at least part of the smaller discrete patch represents the course taken by fibres projecting from nerve cells in nucleus anteromedialis in their radiation towards the cingulate cortex, for it is seen only in the cases showing a primary lesion in the cingulate gyrus and a secondary lesion in the anteromedial nucleus. As will be discussed in a later section, the possibility cannot be excluded that this patch, at levels where it lies adjacent to the subcallosal bundle, represents also degeneration in fibres of the superior occipito-frontal fasciculus; but there is no evidence in the literature which would suggest that elements which move ventrally into the internal capsule need be differentiated from association tracts.

These observations confirm the current view that the anterior thalamic radiation in the anterior limb of the internal capsule remains medial, but require modification of the view that it remains, in its entirety, ventral—for whereas the fibres projecting to the orbital region do remain within the ventral half of the capsule, those radiating to the other prefrontal regions definitely shift into the dorsal half of the capsule.

The conspicuous demyelination contrasts curiously with Crouch's (1940) failure to identify such degenerated tracts by Marchi method in monkey experiments.

Our experience shows that cresyl violet staining of glial cells is, in cases

PLATE I

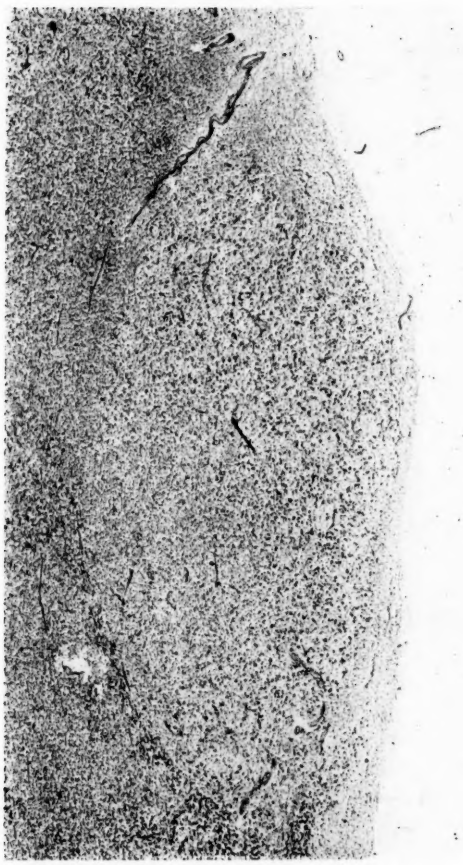

FIG. 17 (*Case* 4) (Left) Bl.VI, 406.—Nerve-cell loss and glial proliferation in lateral part of anteromedial nucleus (Nissl stain × 17), cf. diagram fig. 4. The denser gliosis lateral to the anterior nuclear complex is due to degeneration in the dorsomedial nucleus and the anterior thalamic radiation.

To illustrate article by A. Meyer, E. Beck and T. McLardy.

PLATE II

FIG. 18 (*Case* 5) (Right) Bl.VI, 494.—Nerve-cell loss and glial proliferation, densest in pars magnocellularis and less pronounced in the medical and central portions of pars parvicellularis, of the dorsomedial nucleus (Nissl stain × 17), cf. diagram fig. 10.

To illustrate article by A. Meyer, E. Beck and T. McLardy.

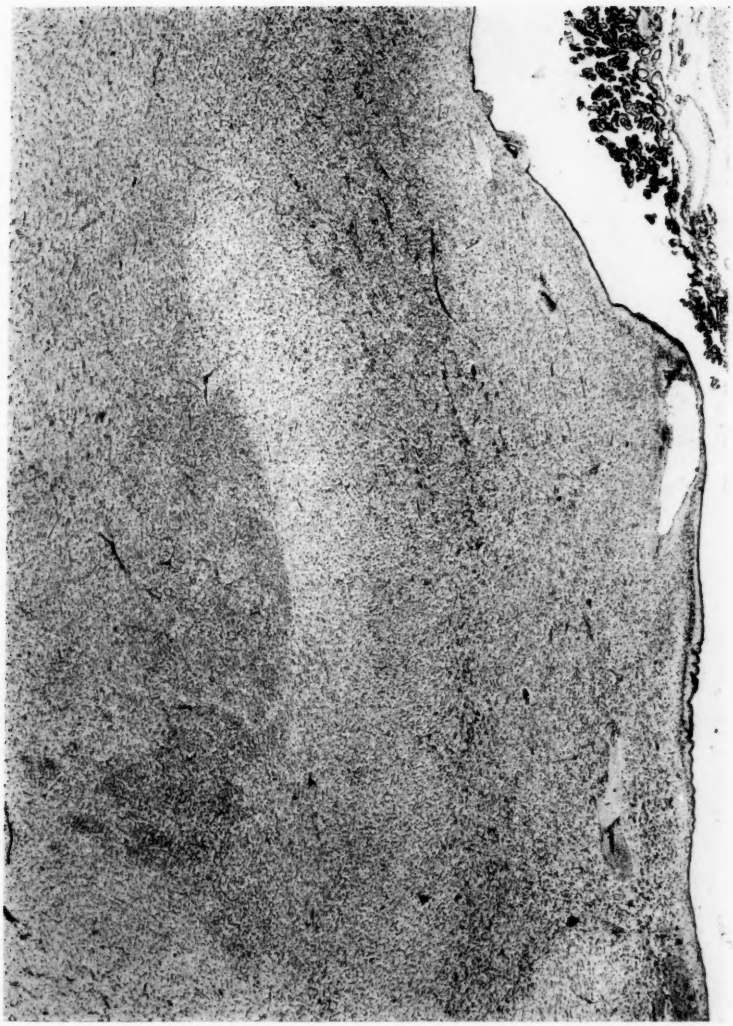

FIG. 19 (*Case* 5) (Right) Bl.VI, 145.—The gliosis shown in figs. 20 and 21 now divided into the thalamo-frontal portion traversing Vam and the fronto-pontile portion continuing down the internal capsule (Nissl stain × 17), cf. diagram fig. 16.

To illustrate article by A. Meyer, E. Beck and T. McLardy.

PLATE IV

FIG. 20 (*Case* 5) (Right) Bl.VI, 295.—The gliosis representing degeneration of the fronto-pontile tract radiating into the most medial segment of the pes pedunculi (Nissl stain × 17), cf. diagram fig. 16.

To illustrate article by A. Meyer, E. Beck and T. McLardy.

PLATE V

FIG. 21 (*Case* 9) Bl.VI, 394.—Gliosed patch in the subthalamic nucleus (Nissl stain × 14), cf. diagram fig. 13.

To illustrate article by A. Meyer, E. Beck and T. McLardy.

PLATE VI

FIG. 22 (*Case* 5) (Right) Bl. IV, 95.—Gliosis in the capsula externa, most dense adjacent to the putamen (Nissl stain × 17), cf. diagram fig. 16.

To illustrate article by A. Meyer, E. Beck and T. McLardy.

PLATE VII

FIG. 23 (*Case* 5) (Right) Bl.IV, 95.—Gliosis in the region of fasciculus cinguli (Nissl stain × 17), cf. diagram fig. 16.

To illustrate article by A. Meyer; E. Beck and T. McLardy.

of over six weeks' survival, an effective method of tracing degenerated tracts. We find also that the longer the survival period the more conspicuously the glial sclerosis stands out. The Holzer stain for glial fibres has also been used in all our cases but has not proved consistently successful.

Prefronto-Pontile Tracts.

In all except Case 3 the remainder of the large gliosed patch described at the beginning of the preceding section when followed posteriorly passes on down the internal capsule. It runs just lateral to the reticular nucleus (fig. 16F) until at the level of the zona incerta it swings ventrally into the medial segment of the pes pedunculi (figs. 16G, H and 20). In all but Cases 4 (Right) and 9, the whole of this gliosis has reached the peduncle just as the anterior tip of the subthalamic nucleus appears in the sections.

In Cases 9 and 4 (Right) at least part of the gliosis appears to pass into the subthalamic nucleus—for in Case 9 a number of almost cylindrical, clear-cut, sclerosed patches stretch from the dorsolateral tip of the nucleus through 200 sections to its ventromedial margin (figs. 13 and 21)—while in Case 4 (Right) a less sharply defined patch stretches from the dorsomedial tip of the nucleus for 100 sections to its ventromedial aspect. Nerve cells are completely absent throughout these patches. Elsewhere in the nucleus in Case 9 all structures appear normal, whereas in Case 4 (Right) there is a mild degree of gliomesodermal reaction which could be a part of the Wernicke changes found elsewhere in this case only. In both cases the caudalmost part of the sclerosis lies immediately adjacent to the lateral part of the substantia nigra; but no changes are distinguishable in the substantia nigra in either case in Nissl, Heidenhain or Holzer stained sections. There is no spacial relationship of the sclerosis to the red nucleus.

In Cases 5 (Right) and 10 where serial sections continue into the pons, the peduncular gliosis can be followed until seen to terminate among dorsomedially situated nerve cells in the anterior pons (fig. 16I). These cells show a considerable degree of shrinkage and nuclear pyknosis but there is no evidence of cellular loss. In Case 9, the only other case having (non-serial) pontine sections, no gliosis is to be found in the pons.

Heidenhain preparations show very considerable demyelination throughout the successive sites of the gliosis. Holzer preparations reveal no definite gliosis.

Discussion.

It is suggested that these appearances represent essentially, in all except perhaps Case 9, degeneration in the prefronto-pontile (Arnold's) bundle.[1]

The precise origin of this cortico-pontile tract has not been definitely established even in animals. All using the Marchi method in monkeys, Ferrier and Turner (1898) placed the origin anterior to the electrically excitable cortex; Mettler (1935) placed it in area 9 only; Levin (1936) related it to areas 9 and 10; whereas Sunderland (1940) ascribed it to area 6, after

[1] Only in Case 4 was the lesion in area 8 sufficiently caudal to have possibly involved the cortico-nuclear tract from the frontal eye field.

excluding areas 8 and 9, but not 10. Our findings so far tend to point to origin in area 10 in man. Thus in Cases 5 (Left and Right) and 6 which show degeneration in the tract area 10 was directly affected by the primary lesion and, perhaps more important, in Case 3 which had no involvement of area 10 there is no degeneration in the tract. In the other cases the position is more obscure. Obviously further evidence is required to clarify the question of origin.

The termination of Arnold's bundle has been somewhat less disputed. The observations of Ferrier and Turner (1898), Mettler (1935), and Levin (1936) agree with our findings in Cases 5 (Right) and 10 that at least part of the tract terminates in dorsomedially situated pontile nuclei. These authors all state, however, that part of the tract also terminates in the substantia nigra. We have not been able to trace any degeneration into this nucleus, although, as stated above, the sclerosis in the subthalamic nucleus in Cases 9 and 4 (Right) lies adjacent to the lateral part of its rostral tip, and in Case 9 no gliosis appears to reach into the pons.

It would be tempting to think that the sclerosis in the subthalamic nucleus in Cases 4 (Right) and 9 might indicate the existence of some fibres connecting that nucleus with the cortex, especially area 44 which is affected by the primary lesion in only these two cases. There is, however, scanty evidence in the literature of any such connection. Ramon y Cajal (1911) described as ending in the subthalamic nucleus, collateral fibres from the internal capsule which he thought were most probably cortical in origin. Mingazzini (quoted by Kodama, 1927) found the medial third of the nucleus very degenerated after extirpation of a dorsolateral portion of the frontal cortex in a Cercopithecus monkey. Kodama (1927), in dogs, observed some fibre bundles to split off from the most medial aspect of the fronto-pontile tract, traverse the medial part of the subthalamic nucleus in anteroposterior direction, and emerge again to course into the pons. He was unable to determine whether any fibres terminated in the nucleus. Roussy and Mosinger (1935) in a review of the subthalamic region mention that some authors report having observed fibres radiating from the cortex to the subthalamic nucleus through the posterior limb of the internal capsule, but that the existence of these is contested by various other authors. Papez (1942) makes no mention of a cortico-subthalamic tract in his review of "fibre connections of the basal ganglia," but does describe a subthalamico-peduncular tract. Until further evidence is available, it is not possible to decide whether the sclerosis in our cases represents a transneuronal degeneration due to section of corticofugal fibres, a retrograde degeneration of cortico-petal fibres from subthalamic nucleus cells, or simply a coinci-

dental lesion. It is difficult to conceive these patches as representing sclerosis in aberrant fibres of the fronto-pontile system, as suggested by Kodama, since the occurrence of such an apparently rare phenomenon in two out of eight cases would be highly improbable.[1]

Long Association Tracts.

Only a few preliminary remarks about the long association tracts are intended at the present juncture as neither the review of the literature, some of which is not easily accessible, nor the actual investigations, are complete. As far as their anatomical and pathological aspects are concerned, these fasciculi have received only scant attention of late years, but there was a lively discussion of them in the older literature (by Muratoff (1893), Bechterew (1899), Dejerine (1895), Probst (1903), Cajal (1911), Niessl von Mayendorf (1919) and others).

Bechterew (1899), for instance, in his textbook illustrates Marchi degeneration of the fasciculus cinguli and the subcallosal bundle in a dog after a lesion of the frontal lobe. Whether the degeneration in the external capsule shown in his fig. 535 corresponds to the fasciculus uncinatus of higher animals remains to be seen, for Mettler (1935) mentions that even in macaques this fasciculus is not yet a compact fibre band. As regards the superior longitudinal fasciculus Bechterew states that, after destruction of frontal cortex of experimental animals, degeneration can easily be demonstrated in it. It is, however, not illustrated in his fig. 535, or elsewhere.

Whatever degeneration is found in these fasciculi it is never traceable along the entire length of the tract. This has given rise to doubts as to whether any of them really represent long association tracts (cf. particularly Niessl von Mayendorf, 1919). Rosett (1933) using his dissection and cast technique comes to the conclusion that at least the subcallosal bundle is not an association system nor a radiation of the caudate nucleus (as believed by Sachs, 1893, and Kodama, 1927). He maintains that its fibres, derived from frontal and prefrontal regions, course uninterruptedly through the caudate nucleus into the pes pedunculi as cortico-pontile and cortico-spinal fibres.

[1] In Case 9 it is evident from the primary lesion and from the absence of secondary degeneration in nucleus ventralis anterior that there is almost certainly no damage to the cells or projection fibres of area 6, from which a cortico-subthalamico-rubral tract has been described as occasionally running through the subthalamic nucleus. Possible relationship to the prefronto-mesencephalic tract remains to be investigated.

More recently Mettler (1935, 1942a) has investigated by the Marchi method the effects on these tracts of prefrontal lobe lesions in macaques. As mentioned above, he finds the fasciculus uncinatus to be only diffusely developed, but is able to trace a degeneration from the inferior frontal gyrus travelling, for the most part, in the extreme capsule and contributing fibres to the claustrum and the superior temporal gyrus-insula complex. The superior longitudinal fasciculus is likewise not yet definitely organized. He believes its origin to lie in the inferior and middle frontal gyri. Some of its fibres degenerate. The cingulum, which he considers to contain fibres travelling in both directions, displays slight degeneration. As regards the fasciculus subcallosus, he reports degeneration in a descending portion and the ventral part of a subcallosal portion, both of which he regards as constituted largely of fronto-occipital fibres having origin in medial prefrontal regions of the cortex; and also in a basal portion which he believes consists essentially of fibres coursing from area 9 to the caudate nucleus. In addition, he finds degeneration of antero-posteriorly orientated fibres in an occipito-frontal fasciculus which corresponds closely in position with Dejerine's (1895) occipito-frontal tract situated just lateral to the subcallosal bundle and by some of the older authors identified with the latter. The degeneration of all these bundles could be ascertained for only short distances, and never for more than half the brain length.

In his textbook on neuro-anatomy, Mettler (1942) in fig. 91 illustrates the human brain as possessed of a superior frontal fasciculus made up of a superior occipito-frontal fasciculus lying within the most medial portion of a superior longitudinal fasciculus, and a more ventrolateral arcuate fasciculus. In this diagram the superior occipito-frontal fasciculus is shown in a position much dorsal to that described in his macaque experiments, and the superior longitudinal fasciculus in a position considerably dorsolateral to that illustrated in his fig. 260. In addition he shows a fronto-occipital (inferior occipito-frontal) fasciculus lying in the capsula extrema dorsal to an uncinate fasciculus which is described as coursing likewise through the extreme capsule. He does not mention the sub-callosal bundle among the human long association tracts, but illustrates it in fig. 264 devoid of a "descending portion."

A new approach to the problem of the long association bundles has been made recently by means of physiological neuronography in monkeys and apes (Bailey, von Bonin, Garol and McCulloch, 1942; Bailey, von Bonin, Davis, Garol and McCulloch, 1944). According to these authors area 8 fires area 18 and vice versa, the impulses travelling assumedly along the superior longitudinal bundle; and there are also two-way connections

between areas 10 and 47 of the frontal lobe and areas 22 and 38 respectively of the temporal lobe, "by way of the fasciculus uncinatus." In addition area 22 is reported to project to area 45, and area 53 to area 37.

Our own observations so far are as follows:—

Uncinate fasciculus.—Of the three cases as yet sectioned sufficiently anteriorly, Case 4 (Right) is unsuitable for study of this bundle because of the primary damage to the external capsule.

Case 5 (*Right*) shows in sections at levels just posterior to the primary lesion a small patch of gliosis lying against the lateral edge of the first strands of the putamen (fig. 16A). Followed in more posterior sections its bulk is seen to be augmented by gliotic radiations from several frontal and orbital gyri (and from the damaged corpus callosum) coursing into it from its dorsal and ventral aspects respectively. Becoming completely separated from the internal capsule by the putamen, and bounded laterally by the claustrum, it comes to lie in the external capsule (figs. 16B and 22). It gradually moves down the capsule, remaining close to the putamen and separated from the claustrum by a band of ungliosed tissue until, as soon as the limen insulæ appears in the sections, it begins to radiate ventrally through the "heel" of the claustrum (fig. 16C). It has dispersed into the temporal white matter just as the anterior commissure is beginning to radiate into that region (fig. 16E).

Case 9 in sections just posterior to the primary lesion shows a heavy patch of gliosis curving from the inferior frontal gyrus (area 44) into the insular white matter. Followed posteriorly into sections showing the claustrum it is seen to lie in the external capsule, forming a much more compactly rounded patch than does the gliosis in Case 5 (Right) and stretching across the whole breadth of the capsule, though without involving the cells of the claustrum. It receives no contribution from orbital or other regions. In the most posterior sections as yet available it is moving gradually ventrally.

Heidenhain preparations in both cases reveal only very faint demyelination in the region of the gliosis.

It remains to be seen whether these gliosed bundles represent something which can be homologized with the fasciculus uncinatus of the literature, whose fibres are described as running essentially in the capsula extrema. The degeneration seems to have been caused in Case 9 by a lesion in and around area 44, but in Case 5 (Right) by a lesion more anteriorly situated, in areas 32, 9, 10, 47, 11 and 12. It is not yet the time, however, to compare these findings with the results obtained from physiological neuronography.

The possible importance of fibre connections between the prefrontal region and the temporal lobe has been emphasized by Spatz's (1937) conception of the functional as well as genetical interdependence of the neopallial basal parts (basale Rinde) of these lobes.

Cingulate fasciculus.—Case 5 (Right) is the only one with suitable lesion and sections for observation of this fasciculus. Sections at levels just behind the primary lesion in area 24 show dense patches of gliosis, one within the medullary white matter of the cingulate gyrus and another

in the neighbouring white matter immediately dorsal to the corpus callosum (figs. 16*a* and 23). These gradually coalesce to form an oval bundle which can be followed in the medullary white matter to a level about 3 cm. posterior to the primary lesion, where it fades out. There is no definite evidence of divergence in any particular direction. Heidenhain preparations show faint evidence of demyelination. No degeneration can be distinguished in the cornu ammonis.

No case was suitable for observation of the fasciculus anterior to the primary lesion.

Subcallosal fasciculus.—None of our cases shows any apparent degeneration in this fasciculus, though it is of interest that in Case 5 (Right) small fasciculi of gliosis appear to originate from it and pass ventrally through the caudate nucleus to join the gliosis in the internal capsule. Whether this indicates degeneration of prefronto-caudate fibres or, as Rosett (1933) has pointed out, fibres passing through the nucleus requires further substantiation.

Superior frontal and inferior occipito-frontal fasciculi.—In the region in which Mettler in fig. 91 of his textbook (1942) illustrates the superior occipito-frontal, superior longitudinal and arcuate fasciculi, we find no evidence of degeneration; nor any in the capsula extrema where he locates the inferior occipito-frontal fasciculus. In the region, however, in which Mettler in fig. 260 of his textbook (1942) illustrates the superior longitudinal fasciculus, and in which Dejerine (1895) describes the occipito-frontal fasciculus, we find that small gliosed patch which in our "Note on the anterior thalamic radiation" we consider to include the sclerosed projection tract of nucleus anteromedialis. It remains entirely possible that it comprises also association fibres which soon disperse and cannot be traced farther backwards.

More definite conclusions will not be drawn until the investigation of more cases is complete, and present methods have been supplemented by Marchi and silver methods in cases with short survival. The material provided by these "human experiments" should then throw definite light upon this controversial, obscure and lately neglected problem of the anatomy of the long association tracts.

Summary.

An anatomical study of 7 leucotomized and 1 lobectomized human hemispheres has led to the following results:—

(1) The anteromedial nucleus of the thalamus projects to at least the pre-callosal part of the cingulate gyrus; the anteroventral nucleus to more

posterior parts of the cingulate gyrus; and the axial orientation of this projection in at least anteromedialis is the same as in animals.

(2) There is some evidence that pars magnocellularis of the dorsomedial nucleus of the thalamus projects to only the medial half of the orbital region of the prefrontal cortex (areas 12 and medial 11), while the portion of pars parvicellularis of the dorsomedial nucleus which lies adjacent to pars magnocellularis projects to the lateral half of the orbital region (areas lateral 11 and probably 47). The dorsolateral portion of pars parvicellularis is found degenerated after lesions of areas 45 and 46 in the inferior frontal gyrus, the ventrolateral portion after lesions affecting the vicinity of area 8 in the superior frontal gyrus. Degeneration of the central portion of pars parvicellularis seems to correlate with a lesion involving areas 46 and 9 (or 10) in the middle frontal gyrus. An anteroposterior axis in the dorsomedial nucleus tends to project to an anteroposterior axis in the frontal lobe.

These observations are not necessarily incompatible with Walker's concept of an axial correlation between the dorsomedial nucleus and the prefrontal cortex in monkeys; but there are some disagreements in detail which necessitate further comparative studies.

(3) Degeneration in nucleus submedius of the thalamus is found to take place after leucotomy. It occurs after involvement of approximately the same areas as those whose damage leads to degeneration in the adjacent ventrolateral portion of pars parvicellularis of the dorsomedial nucleus, i.e. the vicinity of area 8 in the superior frontal gyrus.

(4) The most anteromedial portion of the ventral nuclear complex of the thalamus projects to area 6, and not more rostrally. The anterior part of the reticular nucleus of the thalamus appears to share in this projection to area 6.

(5) The anterior thalamic radiation courses through the tip of the ventral nuclear complex. Thereafter the projection fibres from the medial parts of the dorsomedial nucleus run in the ventral half of the anterior limb of the internal capsule, while the fibres from the central and lateral parts of the dorsomedial nucleus, together with projection fibres from the anterior nuclear complex, run upwards into the dorsomedial half of the anterior limb of the internal capsule.

(6) The existence of a prefronto-pontile tract (Arnold's Bundle) in the human brain is confirmed. It is tentatively suggested that it arises in area 10. It passes down the medial aspect of the anterior limb of the internal capsule and terminates in dorsomedially situated cells of the anterior pons.

The question of termination of elements of the tract in the subthalamic nucleus and substantia nigra is discussed.

(7) Preliminary investigation of long association tracts related to the prefrontal cortex reveals definite degeneration only in fibres which may represent the uncinate fasciculus and fasciculus cinguli. No degeneration is discernible in the subcallosal, superior longitudinal, arcuate or inferior occipito-frontal fasciculi. A sclerosed tract which runs for some distance adjacent to the lateral border of the subcallosal fasciculus is considered to represent part of the course of the projection fibres of the anteromedial nucleus of the thalamus to the cingular cortex, and perhaps also fronto-occipital long association fibres.

We wish to record once again our gratitude to the clinicians (Drs. Harris, McCartan, Rees and Ström-Olsen and Mr. McKissock) who furnished the material utilized in this study, and to Professor Le Gros Clark for his most valuable criticism and interest in the progress of the investigation.

REFERENCES.

BAILEY, P., and BREMER, F. (1938), *J. Neurophysiol.*, **1**, 405.
——VON BONIN, G., CAROL, H. W., MCCULLOCH, W. S. (1942), *ibid.*, **6**, 129.
—— ——DAVIS, E. W., GAROL, H. W., MCCULLOCH, W. S. (1944), *J. Neuropath. Exp. Neurol.*, **3**, 413.
—— —— —— —— ——ROSEMAN, E., and SILVEIRA, A. (1944), *J. Neurophysiol.*, **7**, 51.
BECHTEREW, W. VON (1899), "Leitungsbahnen im Gehirn und Rückenmark," Leipzig.
BONIN, G. VON (1945), "Illinois Monographs in the Medical Sciences," Vol. **5**, No. 3.
CLARK, W. E. LE GROS (1932), *Brain*, **55**, 406.
——and BOGGON, R. H. (1933), *J. Anat., Lond.*, **67**, 215.
—— ——(1935), *Phil. Trans. Roy. Soc., B*, **224**, 317.
——and RUSSELL, D. S. (1940), *J. Neurol. Psychiat.*, **3**, 123.
CROUCH, R. L. (1940), *J. Comp. Neurol.*, **72**, 177.
DARROW, C. W., GREEN, J. R., DAVIS, E. W., and GAROL, H. W. (1944), *J. Neurophysiol.*, **7**, 217.
DEJERINE, J. (1895), "Anatomie des Centres Nerveux," Paris, Rueff et Cie.
FERRIER, D., and TURNER, W. A. (1898), *Phil. Trans. Roy. Soc., B*, **190**, 1.
FREEMAN, W., and WATTS, J. W. (1942), "Psychosurgery," Springfield.
KODAMA, S. (1927), *Arch. Neurol. Psychiat., Chicago*, **20**, 209.
LASHLEY, K. S. (1941), *J. Comp. Neurol.*, **75**, 67.
LEVIN, P. M. (1936), *J. Comp. Neurol.*, **63**, 369.
MAYENDORF, N. VON (1919), *Arch. Anat. Physiol.*, Phys. Abt., 283.
MCCULLOCH, W. S. (1944), *Physiol. Rev.*, **24**, 390.
METTLER, F. A. (1935), *J. Comp. Neurol.*, **61**, 509.
——(1942), "Neuroanatomy," St. Louis.
——(1942*a*), *Res. Publ. Ass. Nerv. Ment. Dis.*, **21**, 150.
MEYER, A., and BECK, E. (1945), *J. Ment. Sci.*, **91**, 411.
MURATOFF, W. (1893), *Neurol. Zentralb.*, **12**, 714.
NORMAN, R. M. (1945), *J. Neurol. Psychiat.*, **8**, 52.

PAPEZ, J. W. (1942), *Res. Publ. Ass. Nerv. Ment. Dis.*, **21**, 21.
PROBST, M. (1903), *Jahr. Psychiat. Neurol.*, **25**, 18.
RAMON Y CAJAL, S. (1911), "Histologie du systeme nerveux de l'homme et des vertébrés," II.
ROSETT, J. (1933), *Arch. Neurol. Psychiat., Chicago*, **30**, 1248.
ROUSSY, G., and MOSINGER, M. (1933), *Ann. de méd.*, **33**, 301.
—— ——(1935), *Rev. Neurol.*, **64**, 637.
SACHS, H. (1893), "Anatomie des Grosshirns," Preuss & Jünger, Breslau.
SHENKIN, H. A., and RUCH, T. C. (1943), *Arch. Neurol. Psychiat., Chicago*, **49**, 780.
SHEPS, G. S. (1945), *J. Comp. Neurol.*, **83**, 1.
SPATZ, H. (1937), *Zeit. ges Neurol. Psychiat.*, **158**, 208.
STERN, K. (1941), *J. Anat., Lond.*, **76**, 302.
SUNDERLAND, S. (1940), *J. Anat., Lond.*, **74**, 201.
WALKER, A. E. (1936), *J. Comp. Neurol.*, **64**, 1.
——(1938), "The Primate Thalamus," Chicago.
——(1938*a*), *J. Anat., Lond.*, **73**, 37.
——(1940), *J. Comp. Neurol.*, **73**, 87.

ABBREVIATIONS.

A	=	Anterior nuclear group.	P.	=	Peduncle.
Am	=	Nucleus anteromedialis.	Put.	=	Putamen.
Av	=	Nucleus anteroventralis.	R.N.	=	Red nucleus.
C	=	Caudate nucleus.	Sb.	=	Subthalamic nucleus.
C.G.	=	Cingulate gyrus.	Sf.	=	Subcallosal fasciculus.
Cm	=	Centromedian nucleus.	S.N.	=	Substantia nigra.
Dm	=	Dorsomedial nucleus.	Temp.	=	Temporal lobe.
F	=	Fornix.	V	=	Ventral nuclear complex.
Gl.P.	=	Globus Pallidus.			
La	=	Nucleus lateralis "a".	Va	=	Nucleus ventralis anteromedialis and anterolateralis.
Lb	=	Nucleus lateralis "b".			
L.G.	=	Lateral geniculate body.			
M.B.	=	Mamillary body.	Var.	=	Nucleus ventralis arcuatus.
M.G.	=	Medial geniculate body.			
M.Th.	=	Mamillio-thalamic tract.	Ve.	=	Nucleus ventralis externus.

(The precise subdivisions of the ventral nuclear complex are not drawn into the diagrams.)

DISEASE OF THE NERVOUS SYSTEM OCCURRING AMONG RESEARCH WORKERS ON SWAYBACK IN LAMBS.

BY

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SWAYBACK is a paralytic disease of newborn and young lambs to which sporadic attention was given by some workers in the Institute of Animal Pathology, Cambridge University, from about 1924 to about 1928. Fuller investigations were begun in 1934 when its pathological nature was established by one of us (Innes, 1936). A full account is given in the papers by Innes (1939), and Innes and Shearer (1940) from which this summary has been taken. The disease occurred in many parts of Britain. In certain areas, viz. Derbyshire, parts of Yorkshire, Buckinghamshire and Wales the incidence in some years was very high, up to 70 to 90 per cent. of the lambs born. In other areas it occurred annually but with a very low proportion of cases. The affected lambs were born from apparently healthy parents, mostly from ewes which had been in an "affected area" for more than one year. The disease occurred in either sex, in single lambs, and both of twins or in all three of triplets. The symptoms consisted of ataxia and paralysis (progressive except in the mildest cases), the lambs either walking with a staggering gait or being completely paralysed and unable to rise. The pathology is a symmetrical cerebral demyelination and degeneration of the motor tracts—ranging in some cases from unmistakable macroscopic gelatinous softening to others in which the liquefaction process is so severe as to cause a porencephalic-like cavitation extending from pole to pole of the cerebral hemispheres. There was thus some justification for comparing the disease to Schilder's encephalopathy bearing in mind the differences which might be seen in the reaction of the immature brain of the fœtal lamb. The enzootic ataxia of lambs in Australia (Bennetts, 1932) was shown later to have the same pathology. It is now certain that the same condition has occurred in certain parts of Peru, Patagonia and the Argentine under the name of "Renguerra" (Innes, 1943), in New

Zealand (Cunningham, 1946), and from clinical descriptions it might well have occurred in Sweden and India, but in none of the other European countries. Schulz (1946) informs us that in South Africa a disease similar to swayback has been identified in a small coastal strip of the country.

All attempts by the workers at Cambridge to transmit the disease failed. They inoculated emulsions of various organs, various parts of the nervous system, and blood into young healthy lambs of differing ages by almost all routes. Lyle Stewart (1932) in this country, Bennetts (1932) in Australia, Gaiger (1917) investigating "Renguerra" in Peru, and Magnusson (1920) in Sweden working with a similar paralytic disease of lambs were all equally unsuccessful in transmitting the condition. The possibility that the disease was a variety of congenital lead encephalopathy was considered by both Innes and Bennetts; it was obvious that in areas where lead has been extensively mined the sheep must have been absorbing the metal in large quantities; the disease, however, also occurred in areas where lead had never been mined. Although this concept was discarded it is still possible that lead may be involved indirectly in connection with the utilization of other trace elements (*see below*). The next step lay in the observation of Bennetts and Chapman (1937) that the disease could be prevented by giving copper supplements to ewes during pregnancy. These observations were confirmed in this country by Dunlop, Innes, Shearer, and Wells (1939). Much further work has been done in this country and Australia (Bennetts and Beck, 1942; Shearer and McDougall, 1944; Eden and Green, 1940) and it is quite obvious that there are still many puzzling features regarding swayback which have never been satisfactorily explained. In particular, we might refer to the fact that the disease apparently is not a copper deficiency *per se* because it occurred in areas where the pasture had a normal copper content. It may be that there is some other factor which interferes with the absorption or with the utilization of copper. In this connection various suggestions have been made, viz. a soil rich in lime stone, the presence of lead, while the recent observations of Dick and Bull (1945) indicate that the presence of molybdenum in the diet may also actively interfere with copper metabolism. The pathogenesis of swayback is thus one of complexity; whatever the causative factors may be they act on the developing myelin of the fœtal lamb with great severity at a time when myelination is at the height of its activity.

This work on swayback demands consideration from the point of its possible application to the study of human disease. Apart from (1) the very rare occurrence of a Schilder's type of encephalopathy in monkeys,

(2) the occurrence of a rare form of demyelinating encephalitis in the moose described by King (1939) and (3) the acute leuco-encephalitis of horses (corn stalk disease) commented upon by Hurst (1940) there is no idiopathic demyelinating disease which occurs in animals with any frequency. The demyelinating diseases occurring in man differ widely but are linked together by the feature common to all of myelin loss whether focal, perivascular or diffuse (Rivers, 1932; Ferraro, 1937; and Weston Hurst, 1936 and 1944). The ætiology of all the demyelinating conditions is obscure and attempts to incriminate viruses, bacteria, toxins, allergy, or a vascular mechanism have failed to carry conviction (Rhodes, 1939). The experimental production of demyelination by a large number of varying agents (Innes and Shearer, 1940; and Weston Hurst, 1944) have simply shown that the lesion could be produced by diverse means. As Hurst says, this appears to exclude any common determinant more narrowly specific than injury to the white matter at one time or another. It has generally been regarded that demyelination is not a common lesion in encephalitis caused by known neurotropic viruses, and apart from the recent work by Margulis *et al.* (1946) no virus has been isolated from any disease of the demyelinating group. The cause of the post-infective type of demyelinating encephalopathy remains obscure. The observations of Weston Hurst *et al.* (1943) on experimental distemper in dogs in Australia indicated that this virus might underlie the demyelination occasionally found in the so-called post-distemper encephalitis, but this has not been the experience of some workers in this country working along the same lines (Innes, 1940).

Disseminated sclerosis is the only common demyelinating disease in man, and in February 1946 we began a study of this disease with the help of specialists in various branches of natural science, including chemists. The problem has been approached from a number of angles including geological, geographical and biochemical, but these studies are not yet complete. However, a new line of approach opened up when it was found that the number of swayback research workers suffering from a disease of the central nervous system had reached remarkable proportions.

Since 1939 neurological disease among those studying swayback had been a subject for comment by a member (J. R. M. I.) of this group of workers, and it has now become evident that no fewer than four of the seven principal workers in a swayback research unit have developed disease of the central nervous system.

Case No. 1, now aged 42, developed weakness of the legs first in 1939, although there were symptoms at least a year earlier. Since then there have been many

attacks of weakness in one or more limbs with partial recovery on each occasion after about a month. Vision has also been affected. He now suffers from ataxic spastic paresis of all four limbs, and two London neurologists have confidently made the diagnosis of disseminated sclerosis.

Case No. 2 was seen by one of us (W. R. R.) in December 1938, when aged 35 years. In June of that year for a period of two days he reported that he had a peculiar sensation in his legs, found walking an effort and could not "chase" the ball at tennis. This cleared up in two days, but two weeks prior to examination there was a return of the same sensation in the legs, the right leg being much more affected than the left. The third, fourth and fifth fingers of the right hand also felt numb. When examined he said that his legs were now again normal, but his fingers were still numb, and that this affected his writing. There had been no other abnormal symptoms. His sister had died of disseminated sclerosis.

On *examination* the only definite abnormality was that on testing sensation in the three affected fingers, marked loss of two-point discrimination and the appreciation of passive movement in the third, fourth and fifth fingers was found, while light touch, pain, hot and cold and vibration sense were fully preserved. There was no weakness or ataxia, and in particular the muscles supplied by the right ulnar nerve were strong. The tendon reflexes were all equal and brisk except the triceps jerks which were both less active. The abdominal reflexes were brisk, and the plantar responses were flexor. The optic discs were normal, and there was no nystagmus. The Wassermann reaction was negative.

The condition was thought at that time to be possibly due to early disseminated sclerosis, and later we are informed that in 1939 he developed retrobulbar neuritis which cleared up in about six weeks. Since 1939 he has felt well except for occasional numbness in the right leg.

Case No. 3. The following specialist's report (dated June 1945) gives the main features of this case:

"I saw this patient last in August 1939, when he was suffering from a localized lesion of the cord, producing slight weakness in the right leg and some thermal disturbance on the left. I diagnosed a focal myelitis, affecting the right side of the cord in the lower dorsal region. His reflexes were exaggerated and the right plantar response was extensor. There was no inco-ordination or any ocular sign, the only other abnormal point being a difficulty in eliciting the abdominal reflexes. The only one definitely present was the left lower.

"The question was raised by him as to whether the condition might have been produced by blows with a tennis ball on his back, but it was impossible to say whether this was the ætiological factor. Apparently he has been very well since this, and though he has had two or three trifling relapses, none was so definite as the primary attack, and he thinks each followed some slight accident.

"He told me that the left eye began to get hazy a few months ago, and Dr. Spence Meighan, with whom I communicated, told me that he had found a central scotoma for red and white, and extending to the periphery in one part of the left eye. On that evidence he assumed that he must have had a retrobulbar neuritis, and that probably it was an early sign of disseminated sclerosis.

"I examined him to-day. He had no inco-ordination of arms or legs. The knee jerks were both very active; there was no ankle clonus and the plantar reflexes gave a flexor response on both sides. I could not detect any abdominal reflexes. Pupils were medium, equal and active, and there was no definite diplopia. There was slight shakiness of the right eye when he looked to the right but no sustained nystagmus. The ophthalmoscope showed the right disc to be normal, but there

was pallor on the temporal half of the left disc, which had not been present when I saw him in 1939.

"In view of the eye signs and the absence of abdominal reflexes, it is quite probable that he is in the very early stages of disseminated sclerosis."

Case No. 4, aged 40, was examined by one of us (W. R. R.) in December 1946. He said that eighteen months ago the left leg began to drag—this lasted for two or three days and then recovered completely. He remained well until six months before examination when the right leg began to drag, and he found his walking had become unsteady. In recent weeks his walking had improved greatly with exercises but was not yet normal. There were no ocular or other symptoms.

On examination the cranial nerves and optic discs were normal. The upper limbs showed no weakness, but the left arm jerks were more active than the right and all were very brisk except the right triceps jerk which was relatively sluggish. The abdominal reflexes gave a very slight response to a strong stimulus on both sides. The knee and ankle jerks were all greatly exaggerated, but much more so on the left where there was ankle clonus. Both plantar responses were extensor. There was no gross weakness or ataxia, but attempts to hop indicated weakness and loss of balance especially on the left. No sensory loss was detected and there was no sphincter disorder.

Cerebrospinal fluid.—A clear colourless fluid. Cells, less than 1 per c.cm.; protein, 30 mgm. per 100 ml.; globulin, negative; chlorides, 747 mgm. per 100 ml.

Discussion.

Over half the members, therefore, of this small group of seven research workers have suffered from signs and symptoms of disease of the central nervous system. In two the signs have advanced little, if at all, for many years, but in all there has been clear evidence of multiple lesions with the remissions and relapses which the neurologist stresses so strongly in the diagnosis of disseminated sclerosis.

All the above four cases are of about the same age; three would seem to have been first affected about 1938-39; these same three are Scottish by birth and upbringing, and two at least were brought up on the Dee-side. Case 2 is a research biochemist who undertook the work associated with the analysis of blood, tissues, soils and pastures during the years of 1934 to 1936 and had little or no contact with the disease in the field: he has been working in another laboratory on the same type of work, but not with swayback since that time. There is also a family history of disseminated sclerosis in his case. Case 1 carried on the work started by Case 2, but in addition was actively involved in the field, handling ewes and lambs, both normal and affected, during the lambing seasons of 1938 and 1939; since then he has carried out a large amount of chemical work in other directions, and has handled swayback material as late as 1946. Case 4 is a laboratory technician, a native of the Fens, who has worked in the same laboratory since about 1925 being first the assistant to Case 2, and

later with Case 1; his main work consists of handling blood, tissues, soils and pastures and assisting in the preparation of routine analyses. Case 3 was an agricultural advisory officer whose main interests before his connection with swayback work were in nutritional problems; during the swayback investigation he was concerned with field inquiries (1937-38-39), would have come in contact with and might have handled, a moderate number of living cases, but had no contact with autopsy work. Two of the remaining unaffected workers were extensively connected with the pathological and field investigations each lambing season from 1934 until 1939, and during this period one (J. R. M. I.) at least must have handled many hundreds of living affected cases and certainly performed autopsies on well over 250.

Each of these four cases would be confidently diagnosed as disseminated sclerosis by any neurologist. It is thus difficult to escape the conclusion that there is an association between their work on swayback and the development of their own nervous disorder. Swayback and disseminated sclerosis are both forms of demyelinating diseases, although it must be stressed that apart from the anatomic myelinoclastic lesions the resemblance ceases . In the case of lambs swayback has its origin in fœtal life and usually proceeds very rapidly in contrast to the later age of incidence, commonly insidious onset, and protracted and fluctuating course of disseminated sclerosis.

The subject therefore requires exploration from a number of angles. First of all there is one factor common to three of the four cases reported, viz. that they were engaged in chemical work for about fifteen years before being affected. This immediately brings to mind the possibility that the conditions under which they worked may have meant special exposure to a "toxic factor" present in such a laboratory atmosphere. This factor could not, however, account for Case 3. Secondly, one must consider the possibility of the swayback workers being infected by the material they handled. This would raise the interesting speculation that the "virus" must be carried by the ewe, causes no ill-health in the pregnant mother and only acts on the fœtal or young lambs in the presence of a copper deficiency.

The possible role of a virus infection in swayback was apparently excluded early in the investigations, but it now seems desirable to repeat transmission work under conditions of a copper deficiency. The recent claims of Margulis, Soloviev and Shubladze (1946) in Russia to have isolated a virus which is neutralized by sera from cases of disseminated sclerosis have revived interest in the possible infective nature of the disease.

Obviously there is much to be said for, and against, any relation between the two diseases. It is not easy to believe that swayback and disseminated sclerosis can have a common ætiology, yet while the causes of the demyelinating diseases remain so obscure no possible avenue should be left unexplored nor any speculation lightly cast aside.

It may be significant that disseminated sclerosis also has a definite geographical distribution. There have been several studies of this subject of which those by Bing (1932) and Sällström (1942) are especially comprehensive. These careful studies indicate that disseminated sclerosis is common in the Scandinavian countries, Germany, Switzerland, France and Britain, but is less common in the Mediterranean countries. Apart from Britain and Sweden no swayback has been reported in any other European country. The coloured races are said to be rarely affected by disseminated sclerosis. Within one country great variations in its incidence are reported, and Bing found the incidence three or four times greater in North than in South Switzerland. South Africa may be an important country from the geographical standpoint for one has often heard that the disease very rarely, if ever, affects a South-African born person of European stock. We have confirmed this view from personal communication with a number of physicians, neurologists and neurosurgeons working in South Africa and feel satisfied that disseminated sclerosis is a great rarity in that country. We have commented on the rarity of swayback in this great sheep rearing country except in one coastal area. It is evident, therefore, that both disseminated sclerosis and swayback have a striking geographical distribution, but there is no clear similarity we yet know of between the distribution of these two diseases except perhaps in South Africa where both are rare. Any attempt therefore to incriminate a common infective agent raises many difficulties including the assumption that the "virus" can only become active under strictly limited circumstances. Further we have no evidence that disseminated sclerosis is unduly frequent in those who handle sheep and mutton.

The fact that trace elements (cobalt, iodine, fluorine, manganese, &c.) have now been proved to be of great physiological importance in man and animals, and in particular that copper is concerned with one demyelinating disease of animals indicates that some attention ought to be paid to the possibility of trace elements being involved in the cause of disseminated sclerosis. It would certainly appear that copper therapy is worth a trial, and some of the affected swayback workers have themselves tried its effect but with uncertain results.

We are, therefore, treating a series of cases of disseminated sclerosis with copper salts. Soft water for cooking and drinking (rain, or distilled water) is advised on the suggestion that some elements in hard water interfere with copper absorption. 1/6 grain copper sulphate (in a capsule with sugar of milk) is given once daily for a month, and once every second day for three months. There is little knowledge regarding the danger of the prolonged administration of copper salts in man, but it may not be without risk. It should be noted that in sheep an excess of copper produces intravascular hæmolysis, anæmia and jaundice, preceded by a very definite rise in blood copper level (Albiston *et al.*, 1940).

We are not yet able to give the results of these trials, but our preliminary impressions are not favourable. It is necessary to emphasize that in attempting to observe a therapeutic trial in disseminated sclerosis any quick improvement should be ignored, and evidence collected over a long period regarding the occurrence of clinical relapses which alone indicate whether or not the disease is still active.

We are indebted to the research workers concerned for their assistance with this study, and to Dr. G. A. Allan and Dr. R. A. Noble for access to clinical notes.

Summary.

(1) Four of seven individuals who worked intensively, in their respective roles, on the demyelinating disease known as *swayback* in lambs, developed a disease of the central nervous system, which is clinically indistinguishable from disseminated sclerosis.

(2) This might be due to an hitherto unidentified occupational hazard of chemical research workers.

(3) This might also indicate that there is some causal connection between swayback and disseminated sclerosis, and some consideration has been given to speculation along these lines, viz. to some common infective agent acting only in the presence of a trace element deficiency.

(4) As swayback is a demyelinating disease and can be prevented by copper therapy, it is apparent that trace element deficiencies should be considered in connection with analagous diseases of man.

REFERENCES.

Albiston, H. E., Bull, L. V., Dick, A. T., and Keart, J. C. (1940), *Austral. Vet. J.*, **16**, 233.

Bennetts, H. W. (1932), *Austral. Vet. J.*, **8**, 137, 183.

——and Beck, A. B. (1942), Bull. Counc. Sci. Indust. Res. Austral., No. 147.

——and Chapman, F. E. (1937), ibid., **13**, 138.

Bing, R. (1932), "Die Multiple Sklerose einst und jetzt," Basel.

CUNNINGHAM, I. J. (1946), *N.Z. J. Sci. Tech.*, **27**, 387.
DICK, A. T., and BULL, L. B. (1945), *Austral. Vet. J.*, **21**, 70.
DUNLOP, G., INNES, J. R. M., SHEARER, G. D., and WELLS, H. E. (1939), *J. Comp. Path.*, **52**, 259.
EDEN, A., and GREEN, H. H. (1940), *Biochem. J.*, **34**, 1202.
FERRARO, A. (1937), *Arch. Neurol. and Psychiat.*, **29**, 1364.
GAIGER, S. H. (1917), *J. Comp. Path.*, **30**, 185.
HURST, E. Weston (1936), *Brain*, **59**, 1.
——(1940), *Austral. J. exp. Biol. Med. Sci.*, **18**, 201.
——(1944), *Brain*, **67**, 103.
——COOKE, B. T., and MELVIN, P. (1943), *Austral. J. exp. Biol. Med. Sci.*, **21**, 115.
INNES, J. R. M. (1936), *Proc. Roy. Soc. Med.*, **29**, 24.
——(1939), *J. Neurol. and Psychiat.*, **2**, 323.
——(1940), *Proc. Roy. Soc. Med.*, **33**, 169.
——(1943), *Vet. Rec.*, **55**, 369.
——and SHEARER, G. D. (1940), *J. Comp. Path.*, **53**, 1.
KING, L. S. (1939), *Amer. J. Path.*, **15**, 445.
MAGNUSSON, H. (1920), *Deut. tier. Wschr.*, **28**, 297.
MARGULIS, SOLOVIEV and SHUBLADZE (1946), *Jnl. Neurol. Neurosurg. and Psychiat.*, **9**, 63.
RHODES, A. J. (1939), *Edin. Med. J.*, **46**, 581.
RIVERS, T. N. (1932), *Arch. Neurol. and Psychiat.*, **28**, 757.
SÄLLSTRÖM, T. (1942), *Acta. Med. Scandinav.*, Supp. 137, p. 1.
SCHULZ, K. (1946), Personal communication.
SHEARER, G., and McDOUGALL, E. I. (1944), *J. Agric. Sci.*, **34**, 207.
STEWART, W. LYLE (1932), *Vet. J.*, **88**, 133.

SOME PHYSICAL ASPECTS OF ENCEPHALOGRAPHY.

BY

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I.—Introduction.

The mind instinctively searches for vital explanations of the phenomena occurring in the human body. However, many seemingly vital phenomena may be explained by simple, known physical facts.

The entry of gas into the lateral ventricles, after it has been introduced into the lumbar subarachnoid space, has lacked an adequate explanation. Some have thought it to be a direct gravitational effect due to flotation of gas through fluid. Others have suggested that vascular pulsation pumps the gas into the ventricles.

The cerebral ventricles fill in the same manner in the cadaver as in the living subject. Hence, it is unnecessary to attribute filling to vascular pulsation. In both the living and the dead gas enters the lateral ventricles when the head is flexed from 55 to 65 degrees [1]. In this posture, the foramen of Monro is considerably lower than the termination of the aqueduct, as may be seen in radiograms taken during encephalography

in this posture. The 3rd ventricle is filled with gas down to the level of the foramen of Monro, and gas passes rapidly into the lateral ventricles. Fluid cannot run upwards through a cavity which remains full of gas hence, in this posture, it was thought that the lateral ventricles must expand to receive gas [1]. No alternative explanation appeared feasible. The diffluent, elastic consistence of the cerebral hemispheres is such as would allow of the expansion of any part of the ventricles which are not circular in cross-section. Such an expansion could occur only at the expense of the volume of blood or cerebrospinal fluid within the skull. Since the pressure of cerebrospinal fluid may remain constant during the early stages of a volume-for-volume replacement of cerebrospinal fluid with gas, it is obvious that collapse of blood-vessels plays little part. It seems probable rather that cerebrospinal fluid is displaced from the cerebral subarachnoid space by the expansion of surface of the hemispheres. The shift of the surface is very slight, for the surface-area of the hemispheres is very large compared with that of the ventricular walls. It was considered that filling depended upon the same factors even when the head was erect. In this posture, however, a downflow of fluid might follow each inflow of gas. Thus, the total volume of gas which enters the ventricles during encephalography may be greater when the head is erect than when it is flexed.

An apparatus was constructed to represent, in as simple a form as possible, the anatomical and physical conditions obtaining during encephalography. This apparatus was described in "Further Studies in Encephalography" [2]. It was found to reproduce *in vitro* the phenomena of encephalography *in vivo*.

Hollow models of the ventricular system provide further substantiation of the theory advanced to account for filling, and allow of further analysis of some factors.

II.—Apparatus—Tubular Ventricular Models.

The two models which have been used are shown in fig. 1. One represents the ventricular cavities and communicating passage-ways. The other has in addition an aperture in the 4th ventricle to represent the foramina of Luschka, and a cavity below the 4th ventricle to represent the cisterna magna. The latter has two apertures, one representing its communication with the spinal subarachnoid space, the other with the cerebral subarachnoid space. In each model apertures are provided in the tips of the occipital horns. In order to facilitate description the appropriate anatomical name will hereafter be applied to the glass counterpart.

III.—Injection of Gas into Rigid and Elastic Ventricles.

A cork through which pass two needles, each fitted with a tap, is inserted into the basal aperture of the simpler model (fig. 2). The ventricles are filled with fluid and stoppers are placed in the occipital apertures. Gas is injected through one needle and fluid allowed to run from the other. The gas fills only the lower chamber and does not pass through the constriction, 4 mm. in diameter, leading to the 4th ventricle (fig. 2*a*). No gas passes into the ventricle, whatever the pressure applied below. Thus, when the closure is rigid, the surface-tension at a gas-fluid junction 4 mm. in diameter is sufficient to prevent downflow of fluid and flotation of gas. This exchange occurs only when the aperture is larger (some 6 mm.). The fluid then runs downwards along the glass walls, around the bubble, as the latter passes distally.

An element of elasticity may be introduced into the closure of the ventricles. Glass chambers, 2·5 cm. in diameter, closed by lax rubber diaphragms (formed by small balloons) are connected to each occipital horn (fig. 2*b*). As before, gas is injected through one needle, the tap in the other needle being open. When the pressure of injection is low bubbles pass through the foramen of Magendie without interruption, and accumulate in the upper part of the 4th ventricles and the lower part of the aqueduct. When the rate of injection is increased or the tap in the other needle partially closed (thus increasing the pressure) the bubbles pass through the aqueduct and 3rd ventricle, to reach the lateral ventricles. If the pressure is maintained and increased gas continues to pass distally. If the injection is stopped gas retreats down the aqueduct and a downflow of fluid occurs around the residual bubble in the 4th ventricle. The greater the volume of gas which has passed distally, the larger the downflow. When gas accumulates in the 3rd ventricle, a similar downflow is observed through the apertures into the lateral ventricles (referred to hereafter as the foramen of Monro). During slow injections an alternating exchange continues until the inflow finally ceases. Less fluid was evacuated when the pressure below was kept above that of the atmosphere. In one experiment 3 c.c. of fluid ran downwards while 8 c.c. of gas entered the ventricles. The fluctuation in size of the balloons during filling and their progressive expansion (to contain the remaining 5 c.c. was readily observed.

When one ventricle is rigidly closed and the other provided with an elastic diaphragm, gas enters only the latter ventricle. This may explain the failure of filling of one ventricle which is sometimes observed during encephalography. Rigidity of one hemisphere, such as might be produced

by a neoplasm, or previous dilatation of one ventricle to a globular form, are possible explanations of this finding. (The increase in pressure which occurs during encephalography is probably insufficient to cause stretching of the ventricular wall.)

It is obvious that the inflow of gas is made possible by the element of elasticity introduced into the closure of the lateral ventricles.

IV.—Effect of Tilting.

In order to imitate marked flexion of the head the anterior horns may be tilted downwards until the foramen of Monro is below the termination of the aqueduct. In this case gas injected under slight pressure displaces fluid downwards through the 3rd ventricle, and then enters the lateral ventricles. No downflow of fluid occurs during filling, as long as the pressure below is maintained, the outflow being completely or partly occluded. In the latter case, gas and fluid escape through the outflow after the injection is stopped. The elastic recoil of tense diaphragms forces fluid from the lateral ventricles into the 3rd ventricle, so that gas is slowly displaced downwards into the zone of lowered pressure. Thus, when the head is well flexed, the volume which enters the lateral ventricles is a measure of the increase in size of the ventricles.

V.—Motive Force.

The motive force under the above conditions is provided by the pressure in the syringe. The bubble moves distally when the rate of injection exceeds the rate of evacuation. This is not the case during encephalography. An increase of pressure in the lumbar theca increases the pressure above the bubble (via the cerebral subarachnoid space) as much as below the bubble. In any case, an endeavour is usually made to keep the pressure constant by the coincident evacuation of fluid.

The following modification ensures that the disturbance of pressure (caused by the injection of gas) has subsided before the gas reaches the cisterna magna. A column of fluid is also arranged to represent the subarachnoid space. An aperture (P fig. 3) is provided for injection of gas near the lower end of one limb (O) of a tall U-tube (ORST). This limb (O), of wide internal bore, represents the spinal subarachnoid space, and leads above to the cisterna magna. The other limb (S) is open to the atmosphere through a tap (T). It serves to maintain the pressure within the apparatus at a chosen level. A tube (K), provided with a tap (L) and a terminal rubber diaphragm (M) is flexibly connected with the cisterna magna through the aperture J, and represents the cerebral subarachnoid

space. The foramen of Luschka (G) is blocked. The rubber-covered chambers (C and M) are removed and the apparatus is filled with water through P, the ventricles being tilted to allow displacement of all the air. The taps T and L are closed, and the chambers (C and M) with their elastic diaphragms are filled with fluid and connected to the already-filled occipital horns (B) and subarachnoid tube (K). The chamber (M) is placed

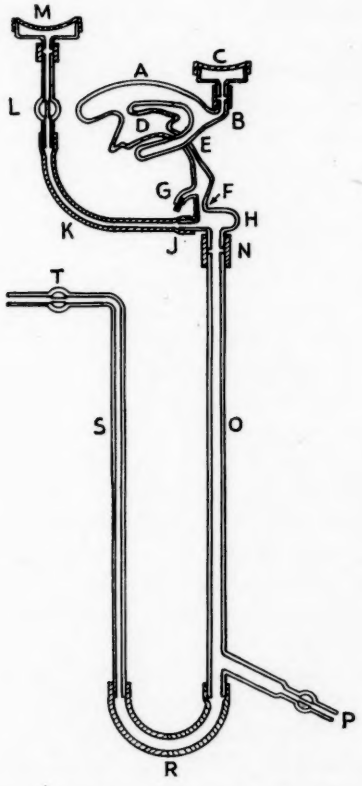

FIG. 3.—Disposition to reproduce some of the conditions obtaining during encephalography. A, the lateral ventricles (the paired cavities being drawn as a single structure); B, occipital horn; C, glass chamber, covered by a rubber diaphragm, attached to occipital horn; D, third ventricle; E, aqueduct of Sylvius; F, foramen of Magendie; G, foramen of Luschka; H, cisterna magna; J, K, L, M, representing the intracranial subarachnoid space; O, spinal subarachnoid space; P, aperture for injection of gas; R, S, T, manometer tube provided with outflow and tap.

at a higher level than the ventricles. The taps T and L are opened to allow a state of equilibrium to be attained and the tap L is again closed.

Gas is now injected at P. A compensatory outflow of fluid occurs through T. Even when a large volume of gas is injected rapidly the disturbance of pressure subsides before the gas reaches the cisterna magna. No gas passes through the foramen of Magendie (F), until the tap (L) is opened. An inflow then occurs whether the tube (K) is open to the atmosphere, or closed by a rubber diaphragm. The inflow is limited by the elasticity of the rubber diaphragm, or when the tube is open above, by the fall of the fluid level in K.

This disposition provides an excellent means of observing the passage of gas through the ventricle. A large volume of gas may be collected in the cisterna magna, and the tap L used to control the rate of inflow. When the system is erect bubbles pass in turn through each constriction and a downflow of fluid is observed through each, following each inflow. The ventricles may be inclined at 45 degrees (utilizing a flexible connection at N). Under these conditions no fluid flows downwards from the aqueduct, lateral and 3rd ventricles, although gas passes in the opposite direction.

These experiments suggest that the pressure of fluid in the subarachnoid space may provide the motive force which displaces gas through the ventricles. Although of complicated shape the ventricular system together with the upper part of the cisterna magna may be looked upon as one limb of a U-tube, the subarachnoid space as the other, the connection being established through the cisterna magna. The upper ends are flexibly closed. When gas is injected, it rises into the lower part of the ventricular limb (the upper part of the cisterna magna), replacing an equal volume of fluid. An unbalanced column of fluid (equal in height to that of the column of gas) now exists in the subarachnoid space. The rise of pressure, in centimetres of water, acting upon the fluid at the distal end of the bubble is equal to the vertical measurement in centimetres of the column of gas. Thus, the bubble moves distally into a region of lower pressure, the space vacated below being filled by an inflow of fluid from the subarachnoid space. The elastic diaphragm C bulges, while M becomes retracted. The elastic recoil of these rubber diaphragms limits the volume of gas which enters.

VI.—A Closer Approach to the Anatomical.

In the anatomical state the cerebral hemispheres separate the ventricular and subarachnoid spaces (as though the upper ends of the two limbs of the hypothetical U-tube were closed and separated by a single elastic

diaphragm). In addition, the subarachnoid space and the ventricular system communicate below through two further apertures, the foramina of Luschka of the 4th ventricle. Modifications to reproduce these conditions were studied in turn.

(i) *Cerebral Hemispheres Represented by Elastic Membranes.*

As previously stated the cerebral hemispheres are of elastic consistency, and in this one respect may be imitated by an elastic membrane. It is possible to arrange an elastic membrane so that it separates the fluid in the ventricles from that in the bell-jar (the subarachnoid space), while a communication exists below through the cisterna magna.

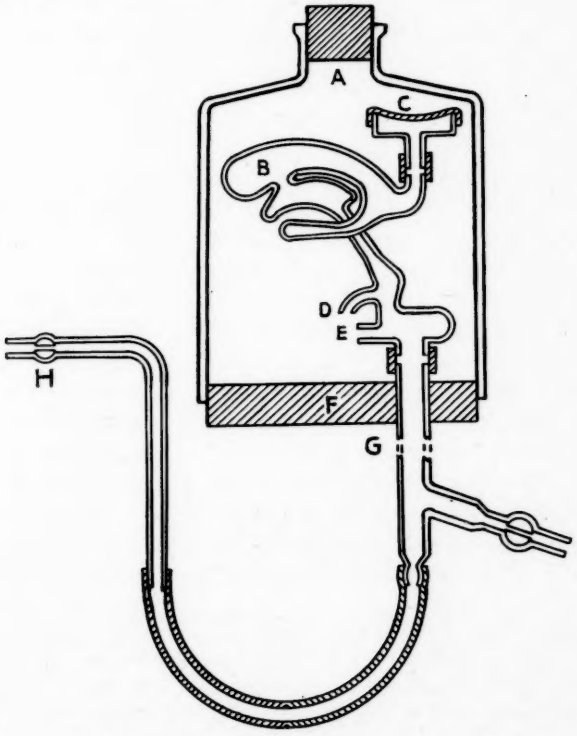

FIG. 4.—Disposition approaching more closely to the anatomical arrangement. A, bell-jar; B, ventricles; C, elastic membranes (representing the cerebral hemispheres) separating fluid in the ventricles from that in the bell-jar (representing the intracranial subarachnoid space); D, foramen of Luschka; E, communication between cisterna magna and bell-jar; F, rubber bung; G, spinal subarachnoid tube; H, tap controlling outflow from manometer tube.

The ventricles (B, fig. 4) with their elastic membranes (C) are placed within a bell-jar (A), the lower end of which is occluded by a rubber bung. The spinal tube (G) passes through the bung to reach the cisterna magna. The whole apparatus is filled with fluid[1] and the stopper inserted in the bell-jar. The effect of injections of gas in the erect and flexed positions may be observed.

(*a*) *Head erect.*—When gas is injected slowly, bubbles traverse the cisterna magna[2] to pass upwards through the foramen of Magendie, the aqueduct and the foramen of Monro. When a fresh bubble arrives soon after the last has passed, the agitation of the newly arrived bubble in the aqueduct gives evidence of the downflow of fluid. At first gas passes freely into the lateral ventricles, but eventually, owing to the downflow failing to keep pace with the inflow, the upward passage of bubbles is impeded. Gas accumulates in increasing volumes in the lower part of the aqueduct and upper part of the 4th ventricle because of the resistance opposed by the gradually expanding diaphragm. Next bubbles begin to accumulate below the foramen of Magendie, separated by a column of fluid from the gas in the upper part of the 4th ventricle. After each influx through the several constrictions a downflow of fluid can be observed, until eventually no more gas passes distally. At this stage small collections of fluid usually remain in the aqueduct and above the foramen of Magendie. When more gas is injected bubbles escape through E into the bell-jar. A meniscus soon forms across E, unless E has considerable diameter (as in the living state), and further downflow of fluid from the bell-jar ceases. Further gas injected accumulates in the spinal tube. Thus, it is seen that expansion of the ventricles occurs as gas enters, while the subsequent elastic recoil produces a downflow of fluid when the pressure below falls. The pressure of fluid in the bell-jar displaces distally the gas which has entered the cisterna magna, 4th ventricle, aqueduct and 3rd ventricles. This is permitted by expansion of the ventricles, which in

[1] The ventricles (B) are attached to the spinal tube (G). The balloon-closed chambers (C) are detached from the occipital horns. The foramen of Luschka (D) and the aperture (E) are blocked, a string being attached to the stopper in E. The apparatus is filled from below as before. The chambers (C) are filled with fluid and connected to each occipital horn. The tap (H) is closed. The bell-jar is thrust down on its bung (F) and the bell-jar is filled with water. The stopper in E is removed by means of the attached string. The stopper is inserted into the bell-jar. The tap H is opened.

[2] In order to allow of analysis gas is delivered directly into the cisterna magna. In the anatomical state this obtains only when the neck is flexed. When the neck is extended gas ascends anteriorly to the spinal cord into the subarachnoid space in front of the medulla.

turn occurs at the expense of fluid in the bell-jar (subarachnoid space), which flows into the cisterna magna.

(*b*) *Ventricles tilted.*—The maximal angle of inclination (flexion) at which gas enters the lateral ventricles under these particular conditions may be determined. The whole apparatus (bell-jar, ventricles and spinal tube) is inclined so that the long axis of the ventricles is tilted forwards about 70 degrees, and a suitable volume of gas is injected. It accumulates in the cisterna magna and spinal tube, but does not pass through the foramen of Magendie. The apparatus is then slowly restored to the vertical position. As the angle lessens gas enters the 4th ventricle, and after a further change of position, the aqueduct and the 3rd ventricle. When large balloons are used, gas begins to enter the lateral ventricles when the inclination is about 50 degrees. The foramen of Monro is then 1 cm. below the termination of the aqueduct. As the inclination is further lessened more and more gas flows into the lateral ventricles, the volume being maximal when the apparatus is almost vertical. The angles are comparable to those found during encephalography. When smaller balloons are used gas enters the lateral ventricles only when the angle of inclination is considerably smaller. These experiments suggest that the ventricles will receive more gas during encephalography when the head is erect than when it is flexed. However, in the erect posture some gas usually enters the subarachnoid space anterior to the medulla. Gas in this region (in the other limb of the U-tube) interferes with the filling of the ventricles, and adds to the discomfort of the procedure. In practice the neck is craned forwards as much as possible, and the head is flexed about 15 to 25 degrees. In this way most of the gas is directed into the cisterna magna. After some 15 to 20 c.c. of gas has been introduced the head is made erect and a further volume of gas is injected. If it is desired to fill the subarachnoid space a larger volume is injected with the head erect or extended—depending upon which regions are to be investigated.

(ii) *Provision of Foramina of Luschka.*

The lateral recesses of the 4th ventricle are two ependyma-lined tubes which pass outwards and downwards from the junction of the middle and lower thirds of the floor of the 4th ventricle; to open by the foramina of Luschka into the lateral recesses of the medullary cistern.

These tubes are some 6 to 8 mm. in length and 2 mm. in diameter. It is difficult to gauge the space available for the transmission of fluid, for each is traversed by a strand of choroid plexus. However, it is probable that fluid passes easily, as it does in the post-mortem state. The

lateral recesses curve around the inferior cerebellar peduncles on each side of the medulla and establish communication between the ventricular system dorsal to the medulla and the subarachnoid space lateral and ventral to it. For convenience, the lateral recesses and foramina of Luschka are represented by a single tube (D, fig. 4). It was found that alterations of the relative levels of the apertures representing the foramen of Luschka and the communication between the cisterna magna and the subarachnoid space (i.e. between D and E, fig. 4) produced variations in the flow of gas. It is therefore important to reproduce the levels found in the brain. In the erect posture, the foramen is some 12 mm. above the passage between the lower part of the cerebellar tonsil and medulla, which is the upper part of the subarachnoid channel between the cisterna magna and the medullary cistern. In the mid-flexed posture the foramen of Luschka is only slightly higher than the above channel, and when the head is fully flexed the foramen is on the same level as, or slightly below, the communicating channel.

(*a*) *Ventricles erect.*—During slow injections gas begins to collect in the 4th ventricle much later when the foramen of Luschka is open than when it is closed, and much more gas passes into the ventricles. In one experiment, when the axis of the ventricles was horizontal and the balloons large, 34 c.c. passed into the ventricles when the foramen was open, and 17 c.c. when it was blocked. Colouring the ventricular fluid assists observation. When the foramen is patent, the first bubbles pass readily through the foramen of Magendie and the aqueduct of Sylvius. However a stage is reached at which a bubble pauses in the upper part of the 4th ventricle. As the injection continues, this bubble increases in size and a further accumulation occurs below the foramen of Magendie. At this stage, it is seen that gas is able to ascend more easily through the foramen of Magendie, by displacing fluid from the 4th ventricle through the foramen of Luschka. Thus, the upward passage through the foramen of Magendie is independent of the flow through the aqueduct of Sylvius, whereas when the foramen of Luschka is closed gas passes through the foramen of Magendie only when gas passes distally in the aqueduct. After each influx of gas, fluid flows downwards from the 3rd ventricle by depressing the bubble of gas in the aqueduct. If the foramen of Luschka be patent, fluid runs outwards into the bell-jar through the foramen, while some fluid flows back into the cisterna magna (through E, fig. 4). When the foramen of Luschka is closed the downflow has not only to depress the meniscus in the lower part of the aqueduct, but also that in the foramen of Magendie. This requires more pressure, hence the elastic recoil of the rubber diaphragms is less complete than when the

foramen of Luschka is patent. Hence less fluid is extruded from the lateral ventricles, and less gas enters. Gas escapes through the foramen of Luschka when the gas-level in the 4th ventricle and the cisterna magna falls below the level of the foramen. If the foramen be high, gas escapes into the bell-jar at an earlier stage of filling than if it be lower, and consequently the ventricles receive less gas. Thus, during encephalography with the head erect, it is possible that gas escapes through the foramina of Luschka into the general subarachnoid space towards the end of filling. On the whole, however, it would seem that the foramina of Luschka materially assists in the filling of the lateral ventricles when the head is erect.

(*b*) *Ventricles tilted.*—When the same balloons are used, the angles at which inflow occurs are the same whether the foramen of Luschka is open or closed. In the flexed posture no downflow of fluid occurs, hence the facilitation which the foramen produces in the erect posture by reducing the resistance to the downflow of fluid does not occur. The pressure of fluid in the bell-jar acting upon gas in the lower chambers is the same whether both D and E (fig. 4) are patent, or E alone. If D is higher than the usual anatomical position of the foramen of Luschka an outflow of gas occurs through it, thus lessening the amount of gas which enters the ventricles in this position.

VII.—Intraventricular Pressure.

A further modification may be used to study the pressure within the ventricles. One occipital horn only is connected to a rubber-covered chamber. A flexible tube (A, fig. 5) is used to connect the other occipital aperture to a tube which passes through the stopper of the bell-jar. This tube is connected to a horizontal length of glass tubing (B) which in turn communicates with a simple water-manometer (C). The outflow (D) of the tube (E) is placed on the same level as the horizontal tube (B). During filling[1] the fluid is brought to the centre of this tube (B). When the out-

[1] The apertures in the fourth ventricle and the cisterna magna are closed by stoppers to which strings are attached. The spinal tube (F), the tube E, the ventricles and the rubber tube (A) are filled with fluid through G. The elastic chamber is connected to its occipital horn at the appropriate time. The tap controlling the outflow (D) is closed. The bell-jar is placed over the ventricles, the strings attached to the stoppers in the foramen of Luschka and cisterna magna being brought out through its neck. The tube (A) is attached to B through the stopper which is not yet inserted into the neck of the bell-jar. More fluid is run into P to bring fluid to the middle of B. The manometer (C) is attached. The bell-jar is filled with water from above, the stoppers are removed from the foramen of Luschka and fourth ventricle by pulling on their strings, and the stopper is inserted into the bell-jar. The outflow (D) is opened.

flow (D) is open the U-tube manometer records zero pressure. The horizontal position of B ensures that variations of intraventricular pressure may be accurately measured.

Gas is injected at G. The injection causes a brief rise of pressure which, owing to the evacuation of an equivalent volume of fluid through D, subsides before the bubble reaches the cisterna magna. As the bubble

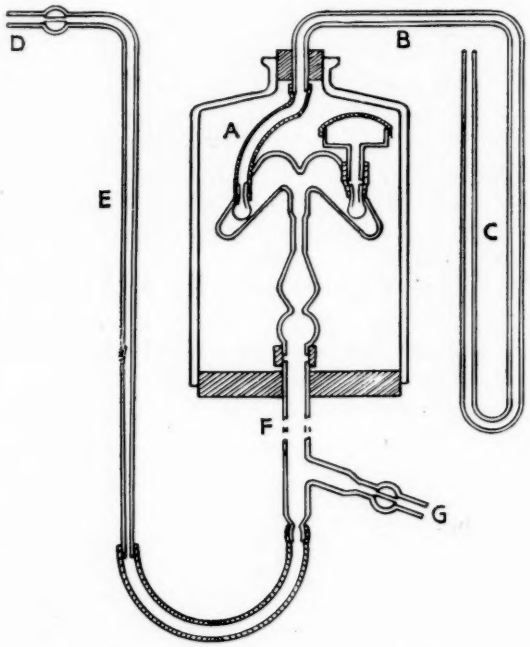

FIG. 5.—Disposition for estimating the intra-ventricular pressure. A, tube connecting one occipital horn, through a horizontal tube B, with a water-manometer C (flexible connecting tubes between A and B, and between B and C not shown); D, outflow of tube E which connects with the spinal tube F; G, aperture for injection.

rises through the aqueduct the intraventricular pressure rises. When the bubble passes completely the pressure falls again to the original level. At a later stage, when gas remains in the 4th ventricle and aqueduct the pressure in the ventricles does not fall to the previous level. The rise in pressure, measured in centimetres of water is exactly the same as the vertical extent of the residual column of gas in the lower chambers. (The initial

rise in pressure is higher, the pressure falling when a downflow of fluid occurs round the bubble.) Thus if the verticle measurement of the residual column of gas be 1 cm., the intraventricular pressure will be 1 cm. of water higher than at the commencement of the injection. If the column be 2 cm., the pressure will be 2 cm. The final rise of pressure, when the ventricles have received their fill, depends upon the vertical extent of the column of gas (or the sum of that of the bubbles). Thus the final rise of pressure is much the same whatever the initial tension of the diaphragm. If the latter be loose, much more gas enters the ventricles than if it be tight.

VIII.—Correlation with Encephalography.

During encephalography, when the neck is flexed, gas rises rapidly to the upper part of the cisterna magna, above the communication between the subarachnoid space and ventricular spaces. The foramina of Luschka, by allowing an escape of fluid from the 4th ventricle facilitates the passage of gas through the foramen of Magendie. In this way gas accumulates in the upper part of the 4th ventricle. The substitution of gas for fluid causes the pressure at the distal gas-fluid junction to be higher than that of the fluid above it. Hence, the bubble travels distally, expanding the lateral ventricles as it does so. The expansion is made possible by the consistence of the cerebral hemisphere. The increase in bulk of the hemispheres (and contained ventricles) displaces cerebrospinal fluid downwards from the subarachnoid space, into the cisterna magna and spinal subarachnoid space. When all the gas enters the ventricles, fluid runs downwards from the lateral ventricles until the pressure within the ventricles has fallen to its original level. If bubbles of gas remain below the downflow is impeded. As filling proceeds the volume of downflow progressively lessens (as more gas accumulates below) and it finally ceases when the column of gas is sufficiently long to balance the rise of pressure within the ventricles. The resistance to further inflow is due to the elastic recoil of the cerebral hemispheres.

When the head is flexed to such a degree that the foramen of Monro is below the level of the termination of the aqueduct no downflow of fluid occurs, and the filling which occurs is due only to the effective column of gas below. When the head is flexed the ventricular limb of the subarachnoid space—ventricular U-tube becomes bent upon itself. The height of the column effective in raising the pressure is the height of the column in the ascending limb minus that of the column in the declivity of the arc. As the flexion increases that of the former diminishes and that in

the latter increases. Thus, as flexion increases the volume which enters the lateral ventricles diminishes until it eventually ceases (at about 55 degrees of flexion).

The downflow of fluid which occurs when the head is more erect also contributes to the greater volume which enters in this posture. In the flexed posture the volume which enters the lateral ventricles is equal to the increase in size of the ventricle. When the head is erect the volume of gas which enters is much greater than the expansion, for an interchange of fluid and gas proceeds until the maximal expansion of the ventricle is produced by the accumulation of gas below.

IX.—Transfer of Gas after Filling.

The models provide a means of studying the mode of transfer of gas from one cavity to another, after gas has been introduced into the lateral ventricles. Gas may be moved rapidly within a lateral ventricle in response to change of posture whether the closure is rigid or elastic, for this cavity is of wide diameter. Gas cannot be transferred from a gas-filled ventricle to a fluid-filled one when the closure is rigid because of the small diameter of the connecting apertures. The transfer can be readily effected when the closure is elastic. When balloons are attached to each occipital horn an interchange of fluid and gas can be effected between the lateral ventricles. If elastic closure be substituted for stoppers in the lower cavities gas can be transferred to the 3rd and 4th ventricles and to the cisterna magna. It is difficult to loculate gas in the 4th ventricle, because of its shape.

Manipulation of the apparatus, with elastic closure, provides an indication of the most satisfactory means of transferring gas from one ventricle to another during encephalography.

(i) *Equalizing the Volumes in the Lateral Ventricles.*

One ventricle is filled with gas and the other with fluid. It is found that fluid flows from the fluid-filled ventricle into the gas-filled one when the former is above the latter. The gravitation of fluid into the lower ventricle is permitted by expansion of the lower balloon, while the upper balloon becomes concave. When the long axis is restored to the vertical gas flows into the upper ventricle to establish equilibrium in this position. Rotation through a small angle produces only a small transfer; rotation through a right angle and back again produces a maximal flow. An equal distribution of gas and fluid can be attained by repetition of this manœuvre. Equalization can be effected even when the fluid level in each ventricle is below the foramen of Monro. Rotation causes fluid to run

to the region of the foramen of Monro in the upper ventricle. Some passes through the foramen, and when the head is restored to the vertical, gas flows in the opposite direction.

Hence, in order to attain an equal distribution of gas during encephalography the patient is placed in the supine posture. The head is then rotated from side to side. The equalization is more quickly effected when the angle of rotation is large, than when it is small. If one ventricle is known to contain much gas and the other but little, rotation through 90 degrees towards the gas-filled side quickly results in equality of distribution.

(ii) *Filling the Temporal Horns.*

After manipulation to secure an equal distribution in the anterior horns, the head is finally turned through 90 degrees to each side and in this way gas may be trapped in the tip of each temporal horn. This provides the most satisfactory method of comparing the position of the tips of the temporal horns during encephalography. In order to show the lengths of the temporal horns the prone patient's head is flexed as fully as possible before an occipito-vertical film is taken. The model shows that the long axis of the temporal horn must be at least horizontal to obtain an adequate filling. In order to obtain effective radiograms it is necessary to raise the patient's chest above the level of the table and to flex the head so that the vertex rests upon the table. The table is then tilted (head downwards) until an adequate posture is attained.

(iii) *Filling Each Lateral Ventricle.*

In order to transfer gas from one lateral ventricle to the other, it is best to begin by equalizing the distribution as described above. The ventricle to be filled is then placed uppermost, the long axis of the ventricles being horizontal. By quickly and repeatedly rotating the ventricles so that the anterior horns turn alternately above and below the horizontal plane bubbles in the lower ventricles are rolled backwards and forwards past the foramen of Monro, and some pass upwards through it, while fluid passes downwards between the passage of the bubbles.

Thus, after axial views have been taken during encephalography the head is turned into a lateral position with the vertex slightly raised. The gas is transferred to the uppermost ventricle by rapid rotatory movements of small amplitude around the vertical axis of the head. To fill the other ventricle the brow is placed uppermost and a few turns through 60 to 90 degrees are made towards the side of the originally gas-filled ventricle. The head is then turned into the lateral position, with the side to be filled uppermost, and the head rocked through some 20 degrees around its vertical axis.

X.—Summary.

Gas does not rise beyond the first constriction which it encounters when it is injected into a glass model of the ventricles.

Gas passes readily through the cavities when an element of elasticity is introduced into the closure of the model.

The flow of gas within glass models is analysed and the findings correlated with encephalograph *in vivo*. It is believed that the lateral ventricles undergo expansion during encephalography. The expansion (and the entry of gas) depends upon the rise of pressure at the distal end of the gas bubble caused by replacement of fluid in the lower mid-line cavities. The increment can be measured by the vertical extent of the column replaced. The expansion of the ventricles leads to expansion of the cerebral hemispheres, and downward displacement of cerebrospinal fluid from the cerebral subarachnoid space. The pressure differential thus created is maximal when the head is erect. Hence the degree of expansion is greater when the head is erect than when it is flexed. This is the only means of entry of gas when the head is flexed sufficiently to bring the foramen of Monro below the termination of the aqueduct. When the head is erect, however, the elastic recoil of the cerebral hemispheres produces a downflow of fluid after each inflow of gas. This also contributes to the better filling in this posture.

The manipulations found necessary to transfer gas from one cavity of the model to another are described and the application of these findings to the radiography of the ventricles is considered.

I am greatly indebted to Messrs. Felton, Grimwade & Duerdins, Pty. Ltd., of Melbourne, for making the glass models, for without these the work would have been impossible.

REFERENCES.

[1] Robertson, E. G. (1941), "Encephalography," Melbourne: Macmillan & Co.
[2] Robertson, E. G. (1946), "Further Studies in Encephalography," Melbourne: Macmillan & Co.

LEGENDS FOR FIGURES.

Fig. 1.—Hollow glass ventricular models. The first represents the ventricles alone and is shown in lateral and anterior aspects. In the second, shown in lateral and posterior aspects, a glass chamber is added to represent the cisterna magna. Two tubes represent the connections of the latter with the spinal and cerebral subarachnoid spaces. A tube representing the foramina of Luschka is added to the fourth ventricle. Apertures are provided in the occipital horns of each model.

Fig. 2.—Comparison of injection of gas into rigid and elastically closed ventricles. The outflow is open in each case.

PLATE VIII

FIG. 1a.

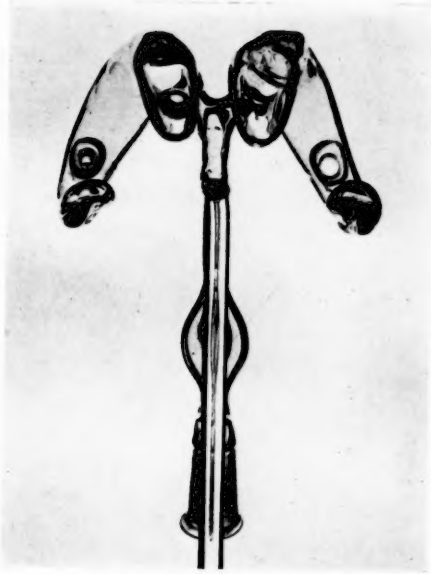

FIG. 1b.

FIG. 1c.

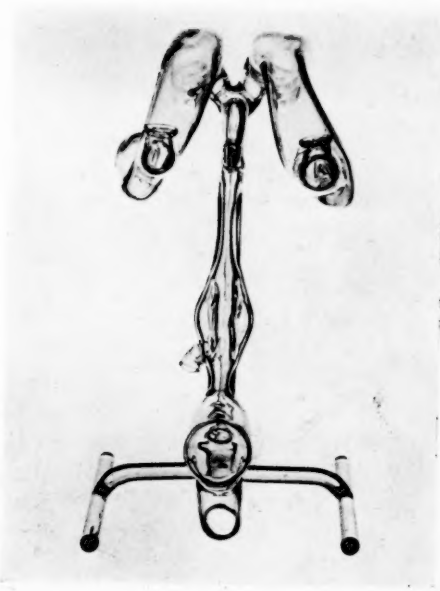

FIG. 1d.

To illustrate article by E. Graeme Robertson.

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Fig. 2.—Comparison of injection of gas into rigid and elastically closed ventricles. The outflow is open in each case.

PLATE VIII

FIG. 1a.

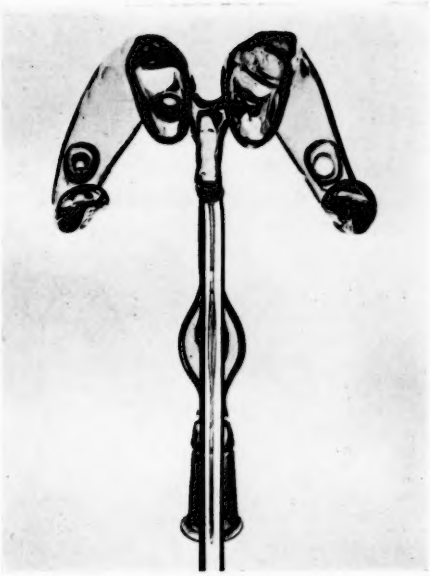

FIG. 1b.

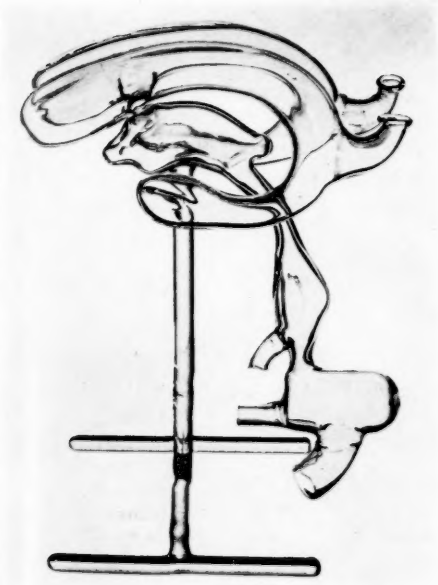

FIG. 1c.

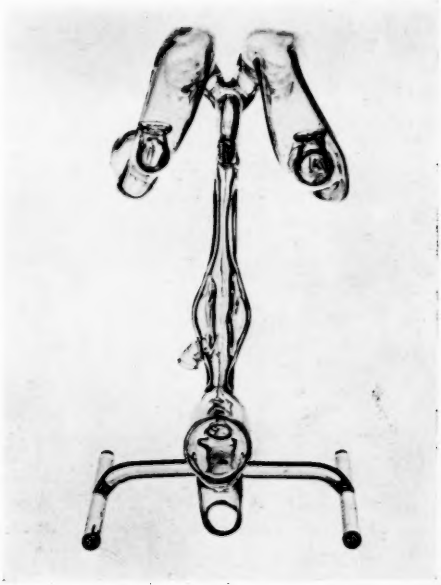

FIG. 1d.

To illustrate article by E. Graeme Robertson.

PLATE IX

FIG. 2a.

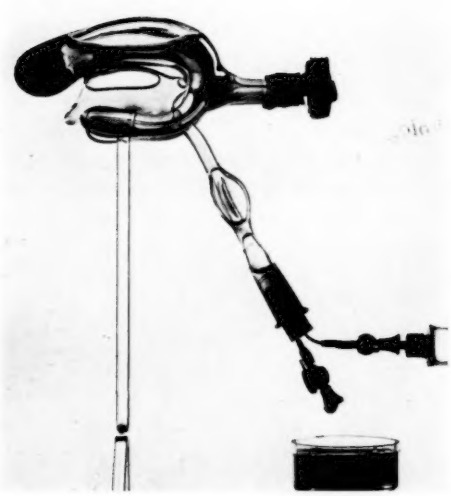

FIG. 2b.

To illustrate article by E. Graeme Robertson.

THE SELECTION AND USE OF AUTOGRAFTS FOR BRIDGING GAPS IN INJURED NERVES.

BY

S. SUNDERLAND AND L. J. RAY.

Department of Anatomy and Histology, University of Melbourne.

IT is generally agreed that gaps in injured nerves are most successfully bridged by the use of autogenous nerve grafts (*see* Sanders, 1942, for a full review of this subject). The choice of such autografts is, with very few exceptions, restricted to the cutaneous nerves and since the diameter of the graft should equal or exceed that of the host nerve the cable variety is necessary to bridge a gap in a large nerve. The selection of cutaneous nerves for this purpose, however, appears to have been governed solely by custom and accessibility. A search of the literature has failed to reveal any systematic study of their morphological features with a view to ascertaining the relative suitability of the different nerves for use as grafts. The present investigation was undertaken to obtain this information and in this connection special attention was directed to the factors influencing: (1) the survival of the graft; (2) the reception and transmission of regenerating axons; (3) the functional maturation of axons; and (4) the restoration of the intraneural fibre-pattern so far as this is possible.

(1) *The morphological features influencing the survival of the graft.*—Though autogenous cable grafts are known to survive in their new environment little information is available concerning the factors upon which this survival depends. Adequate vascularization of the graft is one essential (Tarlov and Epstein, 1945). This requires the rapid and effective penetration of the strands and funiculi by new vessels; thus the bed occupied by the graft should be free from scar tissue and should have a good blood supply. For these reasons the graft should not be separated from the bed by an impermeable membrane. The strands and their contained funiculi should also be of such a calibre that they can be revascularized before central necrosis can occur. The optimum size of these structures is not known but the present study suggests that those provided by cutaneous nerves are rarely so large as to inhibit the rapid and effective vascularization of the graft. The significance of the vascular factor is at present under investigation and no further reference will be made to it in this report.

(2) *The morphological features influencing the reception and transmission of axons.*—The factors controlling the entry of regenerating axons into the funiculi are of primary importance since the latter contain the Schwann tubes and neural fibroblasts (Denny Brown, 1946) which provide the effective framework for the transmission of the axons across the gap. Axons which miss the funiculi enter and end blindly in the interfunicular spaces.

The entry of axons into the funiculi of the graft depends, *inter alia*, on the effectiveness of the union at the ends of the graft and on the arrangement of the bundles in relation to those in the central stump. When grafting a nerve the ideal is to restore completely the funicular pattern. Since this is not possible the best that can be expected is that axons may be directed into whatever funiculi are available. This will be facilitated when the latter are closely packed and particularly when they are large since the funiculi of the central stump will then be opposed to those of the graft and there will be a minimum of interfunicular connective tissue into which regenerating axons can be diverted. The conditions are reversed, however, when the graft is composed of numerous small funiculi which are widely separated by supporting tissue. Here the end to end apposition of funiculi is rendered more difficult or even impossible.

(3) *The morphological features influencing the functional maturation of axons.*—In view of the evidence suggesting a relationship between the functional efficiency of a nerve fibre and its diameter it is important to ascertain the factors which control the diameter of the fibre during regeneration. Sanders and Young (1944), Simpson and Young (1945), and Hammond and Hinsey (1945) have shown that several factors are concerned though only one is relevant to the present discussion, namely, the size of the peripheral Schwann tubes which are to receive and transmit the advancing axons. It has been shown that very small Schwann tubes, such as those of a non-medullated nerve, restrict the development of regenerating fibres, though Simpson and Young (1945) demonstrated that large medullated fibres could inflate peripheral tubes which had contained small medullated fibres. It is possible that the restrictive influences consequent on the shrinkage of tubes in the peripheral stump after long periods of denervation (Holmes and Young, 1942; Sanders and Young, 1942; and Gutmann and Sanders, 1943) would not operate in a fresh autogenous graft where the tubes are rapidly refilled though it occurs in pre-degenerated grafts. "The indications are," wrote Simpson and Young (1945) "that, in man, a piece of cutaneous nerve used as a graft in a motor nerve would not unduly restrict the growth of motor fibres," but they stressed the need for further evidence on these points. On the

other hand, Hammond and Hinsey (1945) state: "It is certain that large myelinated fibres will be restricted in size if the nerve graft contains fibres whose diameters are appreciably smaller than those of the host nerve. Nerves containing large numbers of exteroceptive fibres would be contra-indicated as sources for nerve grafts. Better recovery will probably be obtained if the grafted nerve contains fibres whose diameters are larger than or equal to those of the host nerve." Since one's choice of an autograft is by necessity restricted to the cutaneous nerves, it would be of value to determine the diameters of the fibres in the various cutaneous nerves in order to select the one with the largest fibres.

(4) *The morphological features influencing the restoration of the intraneural fibre pattern.*—The restoration of the intraneural fibre-pattern depends on:—

(*a*) The effectiveness of the union at the ends of the graft by which regenerating axons are directed into the appropriate Schwann tubes. This factor has already been discussed.

(*b*) The funicular pattern and fibre-localization obtaining in the host nerve at the site of injury.

(*c*) The funicular pattern of the graft.

The funicular pattern of the major peripheral nerves is repeatedly modified along the entire length of each nerve by the division, anastomosis and migration of bundles. As a rule the length over which the pattern remains constant varies between 0·25 and 5 mm.—the maximum length without change of pattern is approximately 15 mm. (Sunderland, 1946*a*).

As one ascends the nerve funicular intercommunications result in the gradual dispersal and intermingling of the fibres. At any one level, however, only a few of the bundles are affected so that, over short distances, a minor degree of fibre-shift and mixing occurs with only a slight modification of fibre-localization. Thus fibres representing individual branches pursue a relatively localized course in the nerve for variable distances above the site of branching. It is the summation of changes occurring at successive levels which is responsible for the ultimate widespread intermingling of the different peripheral branch fibres. At any given level the dissemination of distal branch fibres is well advanced, if not complete, while fibres from branches which have just joined the nerve are still concentrated in superficial funiculi. As the latter fibres are traced upwards they, in turn, are redistributed until finally all traces of localization are lost and the constituent fibres of the bundles are arranged in varying combinations though each bundle does not necessarily contain fibres from all the branches. Thus the amount of change in the fibre-localization depends on the length of nerve involved and the level of the examination. Details

relating to the intraneural topography of the radial, median and ulnar nerves have already been provided (Sunderland, 1946*a*).

Since grafting is undertaken only when end to end suture is impossible a considerable length of the nerve must have been lost. This usually will exceed the maximum length over which the pattern remains constant. The opposing nerve ends will therefore present dissimilar funicular patterns though some bundles may correspond since all funiculi are not simultaneously involved in plexus formations. Furthermore the fibre-localization at the central stump will not be identical with that at the distal owing to the redistribution of fibres in the lost segment. The correspondence may, however, be sufficiently close (depending on the level of the injury and the length of nerve destroyed) to warrant its preservation by selecting

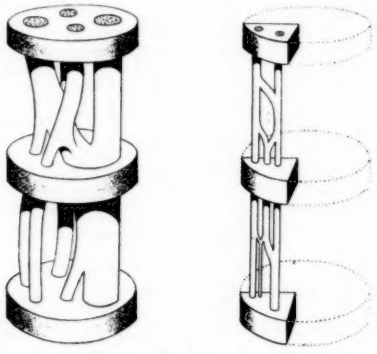

FIG. 1.

a graft with parallel non-anastomosing funiculi and by eliminating torsion in the nerve ends and in the graft. This point will now be considered in further detail.

The alignment of the strands of a cable graft imposes a degree of parallelism in the contained funiculi and the effect of this on the regenerative process may be considered first. Though the sum total of the interfunicular communications occurring in the strands of a cable graft would perhaps be as great as those occurring in a whole-thickness graft there would be less distortion of the fibre-pattern since in the whole thickness graft the interfunicular communications produce a considerable shift of fibres from one part of the graft to another whereas in the cable variety such a shift, no matter how extensive or how complicated, is confined to one strand only and therefore to only a limited sector of the graft (fig. 1). Thus axons growing down one strand of a cable cannot be widely scattered

in their descent while those entering a bundle in a whole-thickness graft may be so scattered. This bestows on the cable variety an advantage which increases as the number of separate strands increases. A stage is reached, however, when such an advantage is offset by the greatly added amount of interfunicular and inter-strand tissue. The most important structures in the graft are the funiculi and these should never be sacrificed.

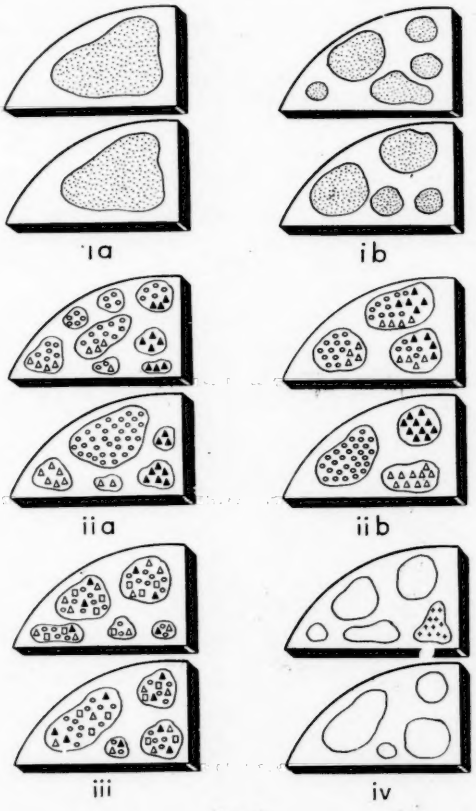

FIG. 2.

In connection with the effectiveness of parallel funiculi in restoring the fibre-pattern one further point requires elaboration. Since a cable strand covers only a portion of the host nerve at each end its funicular pattern can influence only those fibres in the host nerve to which its ends are opposed. It is now possible to compare the influence of a strand composed

of parallel funiculi (here referred to as Type 1) with that of one composed of plexiform funiculi (here referred to as Type 2). In general the funicular pattern in corresponding sectors of the central and distal stumps may conform to one of four types (*see* fig. 2).

(1) The host sector, above and below, contains one or more funiculi (presenting the same or dissimilar patterns) composed of fibres from the same source (fig. 2, i, a and b). A strand composed of plexiform funiculi produces some fibre distortion but this is of little functional significance since it involves only fibres from the same source. The distortion, however, would be greater than that produced by a strand composed of parallel funiculi.

(2) The funiculi in the distal sector contain fibres from different sources but the fibres in each are from the one source (fig. 2, ii, a). Of the funiculi in the corresponding sector of the central stump some contain fibres from the same source and others contain fibres from several of the funiculi in the distal sector; despite this a predominant localization still obtains. Here there is a better chance of restoring the fibre-pattern by the use of Type 1 than by Type 2 strands. Another variant of this arrangement, which gives the same result, is shown in fig. 2, iib.

(3) Where each of the funiculi in the opposing sectors contains fibres from several common sources and all traces of localization are lost, it is immaterial whether Type 1 or Type 2 strands are employed (fig. 2, iii).

(4) Where the sector in the central stump contains a funiculus of fibres not present in the distal there is no way of redirecting them into their old paths in the distal segment of the nerve (fig. 2, iv).

As previously observed the mixing of fibres proceeds as the nerve is traced centrally. Therefore at very high levels the funicular arrangements described in (2), (3) and (4) above will be common, while at distal levels (1), (2) and (3) will predominate. Reference to the diagrams in a paper relating to the intraneural topography of the radial, median and ulnar nerves will provide details of the fibre-pattern in those nerves at different levels along their course (Sunderland, 1946*a*).

Conclusion.—The ideal graft would be one in which the funicular arrangement was identical with that of the destroyed segment in order that, after traversing the graft, the axons would be automatically directed to the appropriate Schwann tubes in the distal segment. In this way the fibre pattern would be fully restored. Though this ideal can never be achieved it is clear that the best graft would be that which has the simplest intraneural pattern—preferably of parallel, non-anastomosing funiculi—so that the axons would be transmitted longitudinally. In this way lateral

deviation of the advancing axons, which tends to distort the pattern, would be minimized. This advantage, however, should not be gained at the expense of tightly-packed funiculi which is the most important feature required of a graft.

Conclusions.

When selecting a cutaneous nerve for grafting the following features should be borne in mind:—

(1) The funiculi should be large and tightly-packed in order to reduce the interfunicular spaces which are responsible for the wasteful dispersal of regenerating axons. The size of the bundles should be compatible with the effective revascularization of the graft.

(2) The graft should be composed of strands of equal length each running the full length of the graft. Each strand should be composed of parallel funiculi or, failing this, the funicular pattern should be as simple as possible.

(3) The graft should just exceed, or at least equal, the diameter of the host nerve. Some overlap is required to compensate for any shrinkage in the graft which would progressively reduce its diameter to a certain minimum value. The rapid entry of axons into the graft would presumably arrest this shrinkage. The overlap, however, should not be too great lest descending axons are carried by interfunicular communications to bundles which, distally, lie external to the margin of the distal stump of the host nerve. In a cable of suitable diameter, the larger the number of strands the greater will be the waste space between the funiculi into which axons may be deflected. Thus the cutaneous nerve selected should be as thick as possible in order to reduce the number of strands required. In this connection it should be remembered that increased thickness is only of value when it is due to funiculi and not interfunicular tissue.

(4) The individual fibres comprising the funiculi should be of large diameter.

(5) The nerve should be readily accessible and constant in position so that it may be exposed rapidly and with confidence. A nerve subject to frequent variations will prove troublesome.

(6) The available length of the nerve prior to and between branches is of considerable importance.

Each strand in the cable should run the entire length of the graft and, if possible, should be free from branches. Frequent branching reduces the thickness of the nerve and, if complicated, shortens its available length. A segment carrying a branch should only be used providing the branch

extends to the distal end of the strand, without itself branching, and can be applied firmly against the parent stem in order to reduce the interfunicular factor. Only by so doing will the funiculi in the branch extend the full length of the graft. If branches are shorter than the full length of the graft funiculi will end abruptly and the axons descending along them will end blindly in the supporting tissues.

In general, cutaneous nerves give few branches while running beneath the deep fascia and only divide freely on entering the subcutaneous tissues. The most useful nerves are therefore those which run long courses beneath the deep fascia and which are constant in structure and mode of branching.

In addition:—

(7) The resulting sensory defect should be minimal in quality and extent and should affect an area where cutaneous innervation is not of great importance.

(8) The resulting scar should not involve a pressure-bearing area.

All these points should be considered when evaluating the end result of nerve grafting.

The Relative Merits of Cable and Whole-thickness Grafts.

A consideration of whole-thickness grafts does not come within the province of this paper but two points are worthy of mention with reference to the relative merits of cable and whole-thickness grafts.

In general the funicular pattern of the major peripheral nerves conforms to one of two main varieties. In one the nerve is composed of numerous small to medium funiculi and in the other of one or two large bundles. Thus the term "whole-thickness" covers two varieties of graft, which correspond with the two varieties of peripheral nerve. The distribution of these types in the radial, median and ulnar nerves has been described (Sunderland, 1946*a*). The multi-funiculated pattern (the common variety) converts the large nerve into what is the equivalent of a collection of smaller strands composed of small to medium funiculi. The funiculi in the cable strands, like those in the large nerve, are held together by the openly-arranged epineurium. The collection of the strands into a cable produces a unit which, excluding the interstrand tissues, differs in no significant respects from a multi-funiculated major nerve trunk. A distinction should only be drawn between whole-thickness and cable grafts when the former is composed of a small number of large funiculi.

Reference has been made to the extensive movement of fibres and bundles which may occur across the nerve in whole-thickness grafts but which is prevented in the cable variety—the significance of this in the regenerative process has been discussed.

Material and Methods.

Dissecting-room material was used and the following cutaneous nerves examined: medial cutaneous of the arm, 4 specimens; medial cutaneous of the forearm, 9 specimens; superficial radial, 18 specimens; lateral cutaneous of the thigh, 10 specimens; and sural, 14 specimens. Two subjects each provided 2 specimens of each nerve (excluding the medial cutaneous nerve of the arm) thus permitting a comparison of the cutaneous nerves in the same individual. A fœtal arm was also serially sectioned at 50 μ for the same purpose; the sections were stained with hæmatoxylin and eosin. The nerves were carefully dissected throughout their length, stained with eosin, cleared in cedarwood oil, and dissected under the microscope. Prior to the dissection blocks were taken at the proximal and distal extremities and at a point about the middle of the nerve trunk. These were prepared in the usual manner, sectioned at 15 μ, and stained with hæmatoxylin and eosin. In this way the relative positions of the funiculi could be ascertained as well as their size, the amount of interfunicular connective tissue and the degree of myelination of the fibres and a check could also be made of the number of funiculi observed by micro-dissection.

Observations.

The General Topography and Available Length of the Nerves.

Details of the topography of the nerves are provided in textbooks of anatomy and will not be given here. The length of the nerves before branching is given in Table III.

Superficial radial nerve.—The nerve runs a constant course beneath muscle and fascia from its origin to the point where it turns posteriorly beneath, or occasionally through, the tendon of brachioradialis prior to piercing the fascia and branching subcutaneously. The branches before the nerve becomes subcutaneous comprise only a few very fine twigs to the radial artery and an occasional branch to the extensor carpi radialis brevis which leaves the nerve within 2 cms. of its origin (Salsbury, 1938; Sunderland, 1946*b*). The nerve has constant landmarks, is readily exposed and is rarely the subject of variation. Gruber has described a case in which it divided beneath the brachioradialis into a lateral branch, representing the normal superficial radial, and a medial which perforated and supplied the brachioradialis before uniting subcutaneously with the lateral branch. The nerve has been reported absent by Hepburn, Versari, Savariaud, Appleton (1911) and Sunderland (1946*c*). In a dissecting-room subject a branch of doubtful functional significance has been observed to pass to the first dorsal interosseous muscle (Sunderland, 1946*d*). The extent of the

sensory innervation of the dorsum of the hand varies but a study of irreparable nerve lesions has shown that the sensory loss is of no importance.

The available length extended from the origin of the nerve to the point where it passed posteriorly beneath the tendon of brachioradialis; it varied from 12 to 20 cm. and was greater in the longer forearms.

Medial cutaneous nerve of the forearm.—The nerve descends beneath the deep fascia for a variable distance (usually as far as the junction of the mid and lower-thirds of the upper arm) before accompanying the basilic vein through an opening in the fascia. It then divides immediately or after a variable delay, into anterior and posterior divisions which branch repeatedly as they descend subcutaneously. The frequency and complexity of the branching below the fascial orifice deprives the two divisions of the nerve of any value as grafts. Twigs may leave the nerve while it is subaponeurotic and pierce the fascia independently. These are usually small and the branching infrequent so that, though the length prior to branching may be greatly reduced, that between branches may be considerable. For example in one specimen the first branch was given off at 5 cm. and did not significantly reduce the diameter of the nerve while the second branch was given off 18 cm. further distally. The length before branching varied from 1 to 20 cm. This nerve is subject to minor variations in its course; the most accurate landmark for identification purposes is the basilic vein which it accompanies. Variable communications with the medial cutaneous nerve of the arm were seen.

The extent of the area innervated varies: It may reach the hypothenar eminence while branches have been observed to replace the dorsal cutaneous branch of the ulnar (Thane). The sensory defect which follows division of the nerve is of no significance.

Medial cutaneous nerve of the arm.—This nerve is inconstant in form, position and manner of branching. It may be replaced by the intercostobrachial nerve or by twigs from the posterior cutaneous branch of the radial while it may communicate with these and with the medial cutaneous nerve of the forearm. It pierces the fascia over the inner aspect of the upper arm at a varying level, usually about the middle, and immediately divides. Twigs also leave the nerve while it is beneath the fascia. It is an unsuitable choice for grafting because of its inconstant course, frequent branching and numerous communications. In some specimens, however, the available length prior to branching varies from 8 to 14 cm. The cutaneous loss resulting from division of the nerve is insignificant.

Sural nerve.—The nerve descends in the mid-line between the heads of gastrocnemius and is enclosed in a fibrous canal outlined by the deep fascia: it is occasionally covered by fibromuscular strands passing superficially between the heads of the muscle. The nerve becomes subcutaneous at the lower limit of the calf at approximately the junction of the mid and lower-thirds of the leg. At this level or further distally it is joined by the sural communicating fibres from the lateral popliteal nerve.

The sural nerve rarely gives branches beneath the fascia so that the length prior to branching or to the receipt of the sural communicating nerve ranged between 14 and 35 cm.—the usual being about 30 cm. Though usually constant in size it is small in some cases when most of the fibres are carried by the sural communicating nerve. The nerve is readily accessible and can be located without difficulty between the heads of the gastrocnemius. The absence of a large bundle in this situation should suggest the presence of a large compensating sural communicating nerve. Though the latter may be used it lacks the advantages of the sural since it is subcutaneous and therefore subject to considerable branching.

The extent of innervation of the postero-lateral surface of the leg and of the internal border and dorsum of the foot varies considerably but the sensory loss occasioned by the removal of the nerve is not sufficiently important to contra-indicate its use.

Lateral cutaneous nerve of the thigh.—Just before or, more commonly, shortly after entering the thigh the lateral cutaneous nerve divides in an unpredictable manner but the following is the usual pattern: (1) one branch is directed downwards and backwards and pierces the fascia 2 to 3 cm. below the anterior superior iliac spine before ramifying in the subcutaneous tissue of the buttock. Its size varies inversely with that of the gluteal branch of the iliohypogastric nerve; (2) two branches descend vertically beneath the deep fascia: the more lateral becomes subcutaneous 5 to 6 cm. below the anterior superior iliac spine and immediately divides; the medial branch runs a subaponeurotic course as far as the mid-thigh. While subaponeurotic all branches give filaments which pierce the fascia independently.

The fibres of this nerve have been observed to run with the femoral nerve and leave the latter below the femoral canal. Schmidt reported this arrangement in 2 of 33 dissections while Griffin described a specimen in which the nerve was replaced completely by the genito-femoral nerve.

The length available in the thigh before division varied from 0 to 8 cm. The pattern of the branchings, together with the great reduction in diameter thereby incurred, considerably reduced the grafting potentialities

of the nerve after branching. The sensory loss following removal of the nerve is of no significance.

Posterior cutaneous nerve of the thigh.—The great complexity and frequency of branching of this nerve beneath the gluteus maximus renders this section quite useless for grafting and would never justify reflection of the muscle. The observations reported below were made on the nerve in the thigh. The nerve descends beneath the deep fascia as far as the pópliteal fossa distal to which it is subcutaneous. While beneath the fascia it gives numerous branches which pass medially and laterally before piercing the fascia. The sensory loss following division of the nerve is without significance. The nerve varies in length, has been described descending in two divisions (Poirier and Charpy, 1901) and has been replaced by the lateral cutaneous nerve of the thigh (Weber and Hildebrandt). The frequency and complexity of the branching greatly reduce both the available length and the diameter of the nerve. The length prior to branching ranged from 1 to 7 cm.

Conclusions.—The superficial radial and sural nerves proved immeasurably superior to the others for grafting purposes. They rarely vary; both present considerable lengths without branching, they may be exposed rapidly and easily owing to their constant anatomical relations and the resultant sensory loss does not impair function. The sural nerve provides greater lengths than the superficial radial but the cross-sectional area in the latter is usually greater and more constant, the sural being subject to replacement, in varying degrees, by the sural communicating nerve.

The topographical variations and the frequency and irregularity of branching (even beneath the deep fascia) render the remaining nerves of little value in comparison with the superficial radial and sural. If, however, they are exposed in the operative field, they should always be examined to ascertain their suitability for grafting.

The Cross-sectional Area of the Nerve and the Amount of Interfunicular Connective Tissue.

Since the effective conducting elements are provided by the funiculi, the thickness of the nerve is of significance only when it is examined in relation to the relative contributions of the funiculi and interfunicular tissues to the total cross-sectional area. The maximal diameter of the various cutaneous nerves and the amount of interfunicular tissue have been correlated in Table I.

Conclusions.—Though in individual specimens the superficial radial

and sural nerves were occasionally exceeded in thickness by others they always provided the thickest strands in which the interfunicular tissue was reduced to a minimum. The lateral and posterior cutaneous nerves of the thigh were particularly unsatisfactory in this regard while the medial cutaneous nerves of the arm and forearm occupied an intermediate position.

The Cross-sectional Area and Number of Funiculi.

Transverse sections of the proximal and distal ends and of the middle portion of each nerve were magnified 25 times and drawn. On the diagrams funiculi with a diameter exceeding 10 mm. and 5 mm. were classed as large and medium respectively while those less than 5 mm. in diameter were classed as small. The size of the funiculi at the three levels in each nerve, together with the corresponding number, are given in Table II. The largest funiculus observed was contained in the superficial radial nerve: its diameters were 0·7 by 0·7 mm.

As a rule the funiculi in any nerve diminished in size and increased in number as the nerves were traced distally. At any level the size and number of bundles were related inversely—the larger the bundles the smaller the number and vice-versa. In general the superficial radial and sural nerves contained the largest bundles: in this regard the former was slightly superior. Next in order of size were those of the medial cutaneous nerve of the forearm while in the remaining nerves the bundles were of equivalent sizes.

No matter how closely the bundles are arranged an increase in their number together with a diminution in their size must lead to an increased amount of perineurium and interfunicular tissue. Therefore, providing the funiculi are closely packed, the total funicular area for the receipt of the axons will be increased as the number of bundles is decreased. This point is relevant only when comparing the relative merits of the superficial radial and sural nerves since it is only in these that the bundles are packed sufficiently closely to validate the argument. The general conclusion was that specimen for specimen, the sural nerve was usually composed of fewer and slightly more closely packed bundles than the superficial radial. The bundles in the latter were, on the other hand, generally larger and the total cross-sectional area of the nerve greater so that the total available intrafunicular area presented by the two nerves was approximately the same. The structure of the perineurial sheath investing the funiculi was substantially the same in all the nerves examined.

The Funicular Plexus.

It was uncommon to encounter cutaneous nerves composed of parallel funiculi running the full length of the nerve though examples were provided by all excepting the superficial radial and medial cutaneous of the arm; the incidence favoured the lateral cutaneous nerve of the thigh. With these few exceptions the funiculi were subject to plexus formations, at irregular intervals, along the entire length of the nerve so that, as a rule, the number of intercommunications was greater in the longer nerves. The incidence of these intercommunications, however, was usually greater in the proximal half of the nerve so that distally the bundles tended to become parallel. The intercommunications in the lateral cutaneous nerve of the thigh were evenly distributed along the nerve. As a result of the plexus formations the funicular pattern varied from level to level; there was no correspondence between right and left sides in the same subject or between the same nerves in different subjects.

Table III gives the number of funicular intercommunications along the length of each nerve which may be regarded as a measure of the degree of parallelism of the bundles. It is difficult, however, to attempt a comparison on this basis of the relative merits of the various nerves since the lengths available differed considerably in each case. Furthermore there is a considerable and unpredictable range of variation in the specimens of any one cutaneous nerve and no nerve had a consistently simpler funicular pattern than any other. If, however, a comparison is made then the following order of priority would be generally applicable: (1) lateral cutaneous of the thigh; (2) posterior cutaneous of the thigh; (3) medial cutaneous of the forearm; (4) medial cutaneous of the arm; (5) sural: and (6) superficial radial. Parallel bundles extending the full length of the nerve were more common in the lateral cutaneous nerve of the thigh because it is only the most distal portion of the main trunk, namely the part in the thigh, which is available. The only safe generalization, however, is that a greater number of funicular intercommunications is to be expected in the longer nerves. Though, for this reason, the superficial radial and sural nerves usually show a greater number of changes of pattern the alterations were never such as to significantly reduce their remaining advantages.

Size of the Nerve Fibres.

The superficial radial nerve consistently contained a slightly larger proportion of fibres of large diameter (12 to 15 μ) than the other nerves in which there appeared to be no significant difference.

Conclusions.

Since no cutaneous nerve provides all the essential features required of a graft it is necessary to select, where possible, those in which the undesirable features are reduced to a minimum. The relative merits of the various cutaneous nerves for grafting have been summarized in Table IV. These have been assessed on the basis of morphological features which influence the reception, transmission and functional maturation of axons, and the restoration of the intraneural fibre-pattern. The present study indicates that the most effective grafts will be provided by the superficial radial and sural nerves which are immeasurably superior to the others. Next in order of suitability is the medial cutaneous nerve of the forearm followed by the lateral cutaneous nerve of the thigh though these have only very slender claims to selection. The medial cutaneous nerve of the arm and the posterior cutaneous nerve of the thigh should not be used if the others are available. Where it is found necessary to use cutaneous nerves which do not conform to the standards required then a reduction in the extent and quality of possible recovery is to be expected.

Summary.

(1) The morphological features of a nerve graft influencing the reception, transmission and maturation of regenerating axons, together with the restoration of the fibre-pattern, have been discussed.

(2) The relative suitability of various cutaneous nerves for the repair of gaps in injured nerves have been investigated and described.

(3) The superficial radial and sural nerves possess qualities which render them more suitable for autogenous grafting than other cutaneous nerves.

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REFERENCES.

Appleton, A. B. (1911), *J. Anat. and Physiol.*, **46**, 89.
Denny Brown, D. (1946), *Arch. Neurol. and Psych.*, **55**, 171.
Griffin. Quoted by Poirier and Charpy.
Gruber. Quoted by Poirier and Charpy.
Gutmann, E., and Sanders, F. K. (1943), *J. Physiol.*, **101**, 489.
Hammond, W. S., and Hinsey, J. C. (1945), *J. Comp. Neur.*, **83**, 79.
Hepburn, Quoted by Poirier and Charpy.
Holmes, W., and Young, J. Z. (1942), *J. Anat. Lond.*, **77**, 63.

POIRIER, P., and CHARPY, A. (1901), *Traité d'Anatomie Humaine*, Tome III. Paris (Masson).

SALSBURY, C. R. (1938), *Brit. Jour. Surg.*, **26**, 95.

SANDERS, F. K. (1942), *Brain*, **65**, 281.

——, and YOUNG, J. Z. (1942), *J. Anat. Lond.*, **76**, 143.

——, ——(1944), *J. Physiol.*, **103**, 119.

SAVARIAUD. Quoted by Poirier and Charpy.

SCHMIDT. Quoted by Poirier and Charpy.

SIMPSON, S. A., and YOUNG, J. Z. (1945), *J. Anat. Lond*, **79**, 48.

SUNDERLAND, S. (1945), *Brain*, **68**, 243.

——(1946*b*), *J. Comp. Neurol.* In the press.

——(1946*c*), To be published.

——(1946*d*), *Anat. Rec.* In the press.

TARLOV, I. M., and EPSTEIN, J. A. (1945), *J. Neurosurg.*, **2**, 49.

THANE. Quoted by Poirier and Charpy.

VERSARI. Quoted by Poirier and Charpy.

WEBER, and HILDEBRANDT. Quoted by Poirier and Charpy.

TABLE I.—THE DIMENSIONS OF, AND THE AMOUNT OF INTERFUNICULAR TISSUE IN, EACH OF THE CUTANEOUS NERVES.

Nerve	*Shape*	*Size : the diameters, in mm., of the smallest and largest specimens*		*Amount of interfunicular tissue*
		Smallest	*Largest*	
Superficial radial	Round becoming oval	1·0×1·5	2·0×2·5	Interfunicular tissue small in amount; funiculi fairly tightly packed but not quite to the same extent as in the sural nerve
Medial of forearm	Round or oval	1·0×2·0	2·0×2·0	Interfunicular tissue intermediate in amount; funiculi more openly arranged than in the superficial radial nerve but more compactly than in the
Medial of arm	Round or oval	0·5×1·0	1·0×1·5	lateral and posterior cutaneous nerves of the thigh
Sural	Round to oval—mostly round	1·0×1·5	2·5×3·0	Interfunicular tissue small in amount; funiculi tightly packed
Lateral of thigh	Round to oval	1·5×1·5	1·5×3·0	Large amount of very loosely arranged interfunicular tissue;
Posterior of thigh	Oval to flat	0·5×2·5	2·0×4·5	considerable separation of the funiculi

TABLE II.—SIZE AND NUMBER OF FUNICULI AT 3 LEVELS IN EACH OF THE CUTANEOUS NERVES.

Nerve	*Proximal end*	*Middle*	*Distal end*
Superficial radial	Large predominating, some medium and occasional small. 2 to 6	Medium to large predominating with some small. 3 to 12	Medium, some small and an occasional large. 2 to 11
Medial cutaneous of forearm	Medium predominating, some small occasional large. 2 to 7	Medium predominat- with some small. 3 to 8	Medium to small. 4 to 12
Medial cutaneous of arm	Medium to small. 2 to 10	Medium to small. 3 to 7	Small predominating, occasional medium. 6 to 8
Sural	Medium predominating, some large occasional small. 1 to 4	Medium predominating, some large and small. 2 to 11	Medium, some small and an occasional large. 2 to 10
Lateral cutaneous of thigh	Medium predominating, some small and an occasional large. 2 to 5	Medium to small. 2 to 7	Small predominating, some medium. 2 to 9
Posterior cutaneous of thigh	Medium predominating, some small and an occasional large. 4 to 8	Medium to small. 4 to 11	Small predominating, some medium. 3 to 10

TABLE III.

Specimen	*Superficial radial*		*Medial of forearm*		*Medial of arm*		*Sural*		*Lateral of thigh*		*Posterior of thigh*	
	L*	N†	L	N	L	N	L	N	L	N	L	N
1	13	12	6	2	—	—	29	17	0	0	2	0
2	14	8	11	4	—	—	32	9	2	0	5	2
3	18	11	20	8	—	—	21	13	0	0	3	0
4	15	9	20	4	—	—	31	26	0	0	1	0
5	19	10	—	—	—	—	14	3	0	0	2	1
6	17	12	—	—	—	—	20	7	3	0	4	0
7	17	8	—	—	—	—	30	0	5	3	2	3
8	17	9	—	—	—	—	28	3	2	0	2	0
9	—	—	—	—	—	—	22	7	8	3	7	2
10	—	—	—	—	—	—	20	0	5	2	5	2
11	12	5	—	—	—	—	32	13	—	—	—	—
12	14	2	—	—	—	—	29	11	—	—	—	—
13	14	9	—	—	—	—	21	5	—	—	—	—
14	13	10	—	—	—	—	35	13	—	—	—	—
15	20	10	5	0	8	6	—	—	—	—	—	—
16	15	1	—	—	—	—	—	—	—	—	—	—
17	13	31	1	0	12	8	—	—	—	—	—	—
18	15	19	5	6	12	12	—	—	—	—	—	—
19	17	3	3	4	14	12	—	—	—	—	—	—
20	19	22	7	15	—	—	—	—	—	—	—	—

L* = the length in centimetres, of the nerve before branching occurred.

N† = the number of alterations in the funicular pattern occurring in this length.

TABLE IV.—THE RELATIVE SUITABILITY OF THE VARIOUS CUTANEOUS NERVES FOR GRAFTING IN TERMS OF ANATOMICAL FEATURES INFLUENCING RECOVERY.

Constancy and accessibility	*Available length*	*Onset and frequency of branching*	*Amount of inter-funicular tissue*	*Total cross-sectional area of funicular surface*	*Alterations of the funicular pattern*	*Diameter of the fibres*
1. Superficial radial	1. Sural	1. Superficial radial	1. Sural	1. Superficial radial. Sural	1. Lateral of thigh	1. Superficial radial
2. Sural	2. Superficial radial	2. Sural	2. Superficial radial		2. Posterior of thigh	2. Remainder
3. Medial of forearm	3. Medial of forearm	3. Medial of forearm	3. Medial of forearm	3. Medial of forearm	3. Medial of forearm	
4. Posterior of thigh	4. Medial of arm	4. Medial of arm	4. Medial of arm	4. Medial of arm	4. Medial of arm	
5. Lateral of thigh	5. Lateral and posterior of thigh	5. Lateral and posterior of thigh	5. Lateral and posterior of thigh	5. Lateral and posterior of thigh	5. Sural	
6. Medial of arm					6. Superficial radial	

ON THE NOTION OF THE "DISCRETE MOVEMENT": A CRITICAL NOTE.

BY

F. M. R. WALSHE.

It is, perhaps, those scientific notions that we take most readily for granted, and receive upon authority with the greatest assurance, that are most apt to repay examination from time to time, and that upon occasion are found wanting when brought to the touchstone of correspondence with facts. The more abstract such a notion the greater the probability that this will be so. Further, in continued currency, abstract ideas seem to harden so easily into concrete facts, and mental constructs come to pass muster for natural phenomena.

It is primarily to discuss a term and to assess the significance of an hypothesis that has become attached to it that this note is written, and as part of a clearing of the ground for a later consideration of the role of the pyramidal system in voluntary movement, to appear in a subsequent paper.

In the physiological literature upon the cerebral motor cortex we may note the increasing use of the term "discrete movement." As far as I can ascertain, this made its original appearance in the classic paper of Leyton and Sherrington (1917) on the excitable cortex of the chimpanzee, orang-utan and gorilla, where it was used as descriptive of those fragmentary movements; e.g. of a digit, or of a segment of a digit, that are evoked upon the application of a punctate faradic stimulus of threshold value and of minimal duration to the excitable cortex of the anæsthetized animal.

The character and the possible significance of the movements so named were clearly expounded by these authors, and no examination of the expression would be called for were it not for the fact that it has recently come to be applied, without any further definition, to a phenomenon of a widely different physiological order: namely, to a particular category of voluntary movements (Tower, 1940, 1944). The expression has therefore now come to have two distinct objects of reference, and the difference between these two is more profound if we hold with Foerster (1931), Fulton (1946) and Hines (1944) that what characteristically emerges from appropriate electrical stimulation of the cortex is a twitch of a single muscle or of a part of a single muscle, and not a movement in the sense that this implies

some element of simple co-ordination (e.g. reciprocal innervation), than if we hold with Leyton and Sherrington (1917) that what are evoked in this way are highly co-ordinated local items of movement.

A confused and equivocal terminology is the fruitful parent of confused and equivocal thinking, and it is necessary to decide whether in a scientific nomenclature we can rightly use the expression "discrete movement" in this loose dual fashion, to ask in what degree the qualifying word is applicable to either category so named, and in particular to consider whether throughout the range of voluntary motor activity as we see it in the normal human subject any specific mode of movement occurs that can accurately be spoken of as "discrete." In other words, is there a physiological process corresponding to the idea embodied in this expression, or is the discrete movement an abstraction, a mental construct, and not a natural phenomenon?

These questions gain their importance in view of Tower's (1940) hypothesis that it is a "unique" and specific function of the pyramidal system to mediate the "discrete" movement, and that movements not of this category result from the activity of extrapyramidal motor systems. It will be seen, therefore, that we have here a clear-cut physiological and anatomical distinction between discrete movements and those deemed not discrete.

At this juncture, clearly, some attempt at definition of the terms "discrete" and "movement" is called for. "Discrete," the O.E.D. tells us, means "separate," "distinct," "discontinuous" and "not coalescent or confluent." It will be noted that no dimensional qualification figures in any of these defining terms, and discreteness is nowhere expressly correlated with amplitude or size. Possibly, it may be thought that "discontinuous and not confluent" most precisely conveys what we have in mind in the general use of the term "discrete," and clearly something that is confluent cannot be discrete. "Movement" might surely seem a term not calling for elucidation. In its general non-technical sense any qualification it may require is supplied by the context in which it is found, but in physiology this looseness of usage is not allowed, and the word has come to connote, not merely a change in the spatial relations of some part, but also, as underlying such a change, a process embodying some element of neuromuscular integration, of which, perhaps, reciprocal innervation is the most fundamental and constant expression.

Tedious as these preliminary considerations may seem, they are essential if we are to avoid, or at least to minimize, that misuse or equivocal use of terms, so much more common in the biological than in the physical

sciences, which in the past has led to so much confusion of thought and to such long delays in the logical evolution of ordered knowledge. In the present connection, for example, if it were to be found that the "discrete" movement is merely an abstraction not corresponding to any observed phenomenon, or the term so equivocal that no correlation between it and any observed phenomenon could be established, then we should have to abandon the notion that it is a specific function of the pyramidal tract to innervate discrete movements, for it would have no meaning.

The Response to Electrical Stimulation of the Motor Cortex Considered as a "Discrete Movement."

The fragmentary movements referred to by Leyton and Sherrington (loc. cit.) as being "discrete" are elsewhere in their paper characterized as "fractional," "separable," "partial," "relatively small," as "local items of movement" and as "in themselves perfect movements." From all of which we may conclude that we are concerned with movements involving notably small fields of musculature and occurring in the otherwise inert musculature of an anæsthetized animal. Yet in such a case only precise electromyography can tell us how extensive is the field of muscular involvement, and this perhaps only when the musculature as a whole shows a background of tonic activity against which inhibition can be as readily discerned as excitation. Such studies have been attempted, for example by Cooper and Denny Brown (1927) and, more recently, by Bosma and Gellhorn (1946), though not precisely with this particular end in view. They afford no confirmation of the view that simple muscle twitches are in question, but, on the contrary, they confirm the complex nature of the motor response and its status as a movement, as originally recorded by Sherrington (1906). We may therefore define the "discrete movement" occurring in response to the electrical stimulation of the motor cortex as *a process employing a small field of musculature and producing a simple phasic movement of a small movable part against the background of a phasically inert musculature in an anæsthetized animal.* It will be noted that in this physiologist's usage a dimensional qualification of the discrete movement has crept in, and this movement has become small as well as separate.

Before leaving the subject a further reference to the hypothesis that the response to cortical stimulation is a simple twitch is necessary. By means of modern methods of stimulation, for example, the thyraton, the condenser discharge and the sine wave current—the details of which it is not here necessary to discuss—it has been claimed to be possible to

obtain finer fractions of movement than were yielded by the simple faradic inductorium used by Sherrington and earlier workers. The twitch hypothesis of the nature of the cortical motor response derives mainly from studies made by these methods. Thus, Wyss and Obrador (1937), working in Fulton's laboratory with condenser discharges, obtained what they describe as a "short twitch," and what Fulton (1946) speaks of as "beautifully discrete responses." But their analysis of the muscular response consisted only in simple inspection and palpation, and in a footnote in their paper they state that "the term 'twitch' is used to describe a brief contraction which may or may not be a twitch in the technical sense." Thus the matter is carried no further, for both method and terminology lack the necessary scientific precision.

Hines also (1944) discusses this question at length, but without any clear conclusions, and makes the following significant statement that "the results of electrical stimulation of the precentral cortex do not demonstrate the ability of that region to produce movement *per se;* rather, they illustrate what the neuromuscular mechanism can do when a current of particular form and intensity is applied to the cortical surface." Here, in this flash of insight and candour, we find bluntly stated the narrow limitations of this experimental method, which, while it does reveal the excitability and the motor function of the precentral cortex, does not tell us anything very clearly of its physiological organization.

Nevertheless, even if adequate electromyographic studies do ultimately reveal that simple muscle twitches can result from electrical stimulation of the cortex, we are still left with a muscular response which may be called discrete in that it consists in a simple phasic contraction of a small field of musculature *against the background of an inert musculature.*

A point of some theoretical interest arises here, for the view that both muscular twitches and movements can arise from cortical action opens up a long vista of discussion about the whole problem of the physiological status of the motor cortex in the co-ordination of movement. It involves the conception of the pyramidal system; the final product of the evolution of the motor system in the brain, as having a simple function of direct innervation of individual muscles; a function not essentially different from that of the ventral horn cell of the spinal cord. It is hard to see how such a notion can be compatible with any view of the central nervous system as an integrated and integrating system, and it must surely involve the abandonment of much that is still generally accepted as firmly established and as fundamental in the teachings of Hughlings Jackson and of Sherrington. The relevant literature shows no sign of recognition that

these implications are inherent in the proposal that the motor cortex innervates muscles and not movements.

Finally, before passing to consider the voluntary movement as showing a specific, "discrete" component, some reference should be made to the profound difference between the motor response to electrical stimulation of the motor cortex and the voluntary movement. The method of punctate electrical stimulation is as artificial and unphysiological a mode of activating the cortex as could be imagined, and to assume that we may directly compare the motor response evoked by this means with a voluntarily induced movement is without warrant. If, despite the dangers thereof, we have recourse to metaphor, the evoking of movement by faradizing a point on the surface of the cerebrum is a kind of forcing of the mechanism, to be likened to the breaking open of a safe. Now we do not reveal the intricate workings of a combination lock by blowing a hole in the safe door or by levering this off its hinges. Perhaps by its very crudity the metaphor may serve to direct attention to the great disparity between a voluntary movement normally mediated in the intact organism, on the one hand, and the response forced out of the cortex by electrical stimulation, on the other. The various and variable factors that go to determine the characters of the latter response under experimental conditions have been discussed by Hines (loc. cit.), and also the influences of the different anæsthetics employed upon the normal spontaneous activity of the cerebral cortex. It appears certain that hitherto we have argued from the results of stimulation experiments to the normal functions of the motor cortex with a freedom that has taken too little account of the very abnormal conditions of experiment. Considerable insight and a very difficult task of interpretation and synthesis are demanded successfully to extract from such experiments any valid conception of normal function, and so far the attempt has been very imperfectly successful.

The voluntary movement, to take but a single feature in which it differs from the cortical stimulation response, is initiated and controlled from its start to its consummation by a constant stream of sensory impulses of diverse sources which reach the cortex. In the mediation of voluntary movements we can hardly think of a motor cortex, *sensu strictiori,* but only, as clinical neurologists have always insisted, of a sensorimotor cortex.

We may conclude, therefore, that even if we agree that the motor response to the electrical stimulation of the cortex is to be called a "discrete movement," this is wholly irrelevant to the quite separate question of whether the voluntary movement is ever "discrete."

THE STATUS OF THE "DISCRETE MOVEMENT" IN VOLUNTARY MOTION.

As was mentioned earlier, the importance of the question of the discrete voluntary movement arises from the fact that Tower (1940, 1944) has proposed that "the one unique function of the pyramidal tract" is "its minute control of discrete movement." Throughout two very important and factually illuminating papers, Tower repeatedly returns to this theme in various and varied phrases, sometimes speaking of this function as "the organized control of discrete movement," sometimes as "an organization for the discrete control of movement." Conversely, loss of this function is said to eliminate all "fine usage," all "discrete usage," and to leave behind only "a limited number of stereotyped components" of movement. But even the latter are not left unimpaired when pyramidal function is abrogated, for they now show "loss of initiative," a raised threshold, and an absence of precision and aim. In Tower's view these defects result from the loss of a secondary pyramidal function of "modulating" these stereotyped components and of lending them speed and precision. It should be added, in conclusion, that the stereotyped components of voluntary movement are postulated as being extrapyramidally innervated.

It is not proposed in the present note to give any detailed critical study of this hypothesis as a whole, but its validity depends upon the phenomenal reality of a category of discrete movements, and this is the problem now under discussion. It will be apparent that this discussion hangs upon the definitions we have to give to the operative terms used: namely, "discrete," "stereotyped," "modulate," "loss of initiative" and "raising of threshold." The first of these we have already considered, but the others are all potentially very equivocal terms and call for precise definition if confusion is to be avoided. How, for example, is the threshold of a voluntary movement raised, and how is the rise determined? What in such a movement is "loss of initiative," if this is an idea different from that of paralysis? And how, finally, does the pyramidal system "modulate" and lend aim and precision to extrapyramidal, stereotyped movements? Surely it can do so only by taking part in the innervation of the extrapyramidal movements. We shall then find that we have lost our category of specifically extrapyramidal movements. Conversely, is it proposed that those discrete movements which it is the prime function of the pyramidal tract to innervate owe nothing to the activity of extrapyramidal neurone systems? Surely not, yet if we admit extrapyramidal participation in them, we have lost our specific category of pyramidally innervated movements.

Now voluntary motion, as all would agree, is the sum of the harmonious co-ordination of both pyramidal and extrapyramidal systems, and this antithesis of "discrete" and "stereotyped," of "pyramidal" and "extrapyramidal," begins to assume a highly artificial appearance, and seems to propose for our contemplation categories that in nature we cannot readily differentiate, or conceive as existing apart from, one another.

We must therefore proceed directly to consider the evidence that there is in voluntary movement, conceived as a whole, a clear-cut distinguishable category that is "discrete" in the sense that it is separate, neither confluent nor coalescent, and that it is small. It is plain that unless the category of movement that we are seeking conforms to these postulates it can have no existence in nature. It is not sufficient that in our minds we can break up an idea of a movement-complex into part ideas, or that we can abstract imaginary components from the whole function: much, for example, as Head and Rivers abstracted the idea of "localization" from that of tactile sensibility and thereupon proceeded to postulate an independent anatomical pathway for the conduction of this idea to the sensory cortex (cf. Walshe, 1942). To do this would be to repeat once again the fallacy of "misplaced concreteness," for we cannot create physiological functions merely by thinking about them, or erect useful physiological classifications that do not correspond to anything in nature.

Perhaps the simplest way to tackle the problem of identifying the specifically discrete component in voluntary movement is to take some familiar action involving an entire limb in complex phasic activities, and to ascertain whether or not we can differentiate discrete and stereotyped components in it. Let us take the use of the upper limb in typewriting.

Here, in changing sequences the digits move up and down upon the keys, while the hand moves to and fro laterally as well as up and down across the keyboard. There is not a muscle in the limb within the reach of observation by palpation or inspection that we do not find to be engaged. Where in this action do we find the "discrete," the "fine" usage, and where the "stereotyped"? I submit that it is not possible to draw a distinction of this order. The co-ordinated muscular activity by which the whole limb is traversed so that the digits may play over the entire length of the keyboard is as fine, as precise and as correct in aim, as the play of the digits themselves upon the keys. In other words, the proximal and the limb girdle muscles are being employed in movements as minutely adjusted as those of the muscles operating the digital movements. The fact is that this action cannot be dissected into discrete and stereotyped components. Piano and violin playing provide comparable

examples, and in the case of the bow hand it might be urged that movements at wrist and elbow surpass in delicacy those of the digits.

It might be objected that the role of the pyramidal system in a movement-complex varies with the form of the complex in question, and that in some instances the action of the pyramidal system may have a "modulating" effect upon the entire combination of extrapyramidally innervated stereotyped components, making a confluent action in which discrete and stereotyped components are merged indistinguishably.[1]

But such an account, while it might save the antithesis between the two categories on paper, would abolish it in fact, for a movement which has become confluent is no longer discrete, while one that takes on the qualities of fine usage and minute adjustment has surely ceased to be stereotyped.

The purpose of this argument is to suggest that (i) in such a familiar action as typewriting two separate categories of movement, discrete and stereotyped, cannot be distinguished, and that (ii) in respect of all the movements making up the total action we note an equal measure of precision, of fineness of adjustment and of capacity for variation.

It appears, therefore, that in our search for the discrete component in voluntary movement we shall have to abandon all the recognized meanings of this term, and to concentrate upon that emphasis on smallness that is a feature in the original usage of the term in physiology. For in this usage it is indeed the matter of size that is the significant one, and the quality of separateness or non-confluence is almost fortuitous, and

[1] How complex is the notion of "modulation" is best indicated by the following quotation (Tower, 1944, p. 170). "The phasic or episodic function (of the pyramidal tract) appears as a specific contribution to individual acts or performances, and often as the entire performance. This enters into all somatic motor activity of any complexity to initiate it or to speed initiation, to confer upon it adjustability in space, which is aim, and modifiability in time or in the course of execution. It contributes the elements of precision, lability, and finish to stereotyped performances. . . ." This is indeed a very striking passage, but, it may be submitted, it would prove extremely difficult to extract from it a clear idea in strictly scientific terms and in recognized physiological categories of the part played by the pyramidal system in the co-ordination of movement. To endow this system with the titles of a number of attributes, as is here done, is not to analyse or interpret its functions. How, for example, can stereotypy and lability inhere in the same movement? How can either quality inhere in a single movement? Surely these terms do no more than express relations of likeness and unlikeness between the component units of a sequence of movements. Indeed, it may be urged that while this passage creates a very vivid impression in the reader's mind, it conveys no clear information.

dependent upon the fact that as a whole the musculature of the anæsthetized animal under experiment is inert. Herein is a point that seems to have been overlooked by those who have carried over the term "discrete" from the experimental laboratory to the study of voluntary movements.

Let us now take a movement instanced by Tower as a characteristic sample of the discrete movement; namely, the approximation of the tips of the thumb and index finger. Here would seem to be a movement as restricted as any to be found in the polymorphic range of voluntary motion in man, and one displaying maximal delicacy of adjustment.

If the observer, having completely bared his arm, holds his hand in front of himself and repeatedly makes the movement of bringing thumb and index finger tips together, he will be able, if the limb be sufficiently spare, to see in phasic action the muscles taking part in this "discrete" movement. He will observe that most of the muscles of the hand and forearm are taking part, and that when he makes the movement forcibly so as to bring the digit tips into firm apposition, still more muscular action becomes evident, although the range of the original willed movement has not increased. In this movement, then, we see that other digits than thumb and index are in motion. The middle and ring fingers show a synchronous flexion and extension of smaller range than index movement, but a motion quite incapable of being inhibited voluntarily. When the thumb-index apposition is forceful, the middle, ring and little fingers all go into synchronous flexion and extension. If now with thumb and index of his opposite hand, the observer grasps the middle finger tip of the moving hand, he will feel as the rhythmic thumb-index apposition goes on that the middle finger strains to take part and cannot be induced to relax. In addition, muscles in the thenar eminence are seen to contract, the flexors and extensors of the digits in the forearm, and also the wrist extensors in phasic synergic action. In brief, we are dealing with a movement necessarily involving four or five digits, and, in the process, most of the musculature of hand and forearm, and the more we examine it, the less discrete it is found to be. If, now, using this nipping movement of thumb and index, we proceed to pick in sequence, and out of a strip of cardboard in which they have been stuck in a row, a number of pins—beginning to right or left of the row and proceeding to the opposite end, we at once bring into phasic action—in addition to the muscles already involved—virtually every muscle in the limb and limb girdle, and we are back again in a situation not materially different from that involved in using a typewriter, except that now, possibly, each component in the movement-

sequence is so nearly identical with its fellows that the entire sequence might be called stereotyped in the O.E.D. sense of "fixed or perpetuated in unchanging form."

These examples show how unreal are these two categories of "discrete" and "stereotyped," how impossible of identification in parts in motion, and how completely they fail by definition to provide any true antithesis for purposes of classification. By no definition can we easily find a voluntary action that is discrete, for even the apparently very restricted movement employs a large field of musculature phasically, and provides nothing for our inspection comparable with the local and apparently "discrete" motor response to cortical electrical stimulation. Nor can we any more effectively differentiate a "discrete" component in voluntary movement by virtue of any specific fineness of adjustment or precision which a hypothetical "stereotyped component" does not possess.

How beautifully precise, for example, is that reflex sequence of movements exhibited by the cat, when dropped in air from any initial posture, in alighting nimbly on its four feet, yet this sequence is wholly independent of pyramidal system activity.

On the other hand, we have only to contemplate the gross disorder of voluntary movement that is called cerebellar ataxy, to appreciate that the pyramidal system is impotent to confer finish, precision or aim on any movement when a subordinate and extrapyramidal component of the motor mechanism is out of action, and we might argue thence that the imparting of these qualities to movement is the specific and "unique" function of the cerebellar system. The fact is, of course, as von Monakow long since pointed out, that we cannot argue *from the symptoms of lesions to normal functions* in this naive fashion.

Finally, we cannot identify these two supposedly qualitatively distinct components of voluntary motion with Hughlings Jackson's "most voluntary" and "most automatic" elements in movement, elements for which he expressly denied *qualitative* distinctions, and for which he postulated no separate anatomical substrata.

It appears, then, that these two terms are wholly inadequate to any analysis of voluntary movement, and that no hypothesis of the role of the pyramidal system in movement can be built upon them. This is not to say that restricted movements performed against the background of a phasically inert musculature are invariably impossible, for we can wink, raise our eyebrows and shrug shoulders, but from these special examples of movement, we cannot erect a constant, specific mode of movement in voluntary motility.

It is perhaps true that few who have written upon the physiology, or upon the disorders, of movement have not at some time employed one or more of these terms, though in clinical writing the word "isolated" has had more vogue than has "discrete." Yet whatever their usefulness in general description, or at a stage in knowledge when precise analysis is not possible, they have no place in the current study of movement—even were they more precisely employed than they now are.

SUMMARY.

It appears that the notion of "discrete movement" arose in connection with the study of those fragmentary local items of movement observed to follow upon the punctate electrical stimulation of the excitable motor cortex of the anæsthetized animal. In this usage, the term has an appreciable measure of descriptive accuracy, whether we regard the movements so obtained as simple "twitches" or as "movements" in the precise senses obtaining for these words in neurophysiology. Such movements are "discrete" in the strict sense of "separate" mainly because under the conditions of experiment the musculature as a whole is phasically inactive.

Voluntary movement cannot be directly compared with the movements arising from electrical stimulation of the cortex, and it does not take place against a background of an inert musculature, for, as Sherrington (1946) has graphically expressed it, "to take a step is an affair, not of this or that limb solely, but of the total neuro-muscular activity of he moment—not least of the head and neck." Hines has put the matter equally forcefully when she says "no violin or piano was ever played with the fingers and hand alone." Nor is all this implied background of movement to be disposed of as merely postural, as providing a medium against which the phasic movement stands out discretely, as it were. The illustrations given earlier in this paper show that this is not wholly so. Thus, the carrying over of the term "discrete movement" from the laboratory to the description of voluntary movement is invalid, for the term is inapplicable within this category of movement, and thus cannot be made the basis of an hypothesis of pyramidal system activities in movement. In addition we have to stress the need not only of a precise, and precisely used, scientific terminology, but also that of distinguishing between abstract ideas and natural phenomena in our analysis, classification and interpretation of the latter. In so far as voluntary movement is concerned, the discrete movement is, I submit, an abstraction hypostatized and not a natural phenomenon. It cannot therefore be a specific function of the pyramidal system to innervate discrete movements.

REFERENCES.

BOSMA, J. F., and GELLHORN, E. (1946), *J. Neurophysiol.*, **9**, 263.

COOPER, S., and DENNY-BROWN, D. (1927), *Proc. Roy. Soc. B.*, **102**, 222.

FOERSTER, O. (1931), *Lancet*, **2**, 309.

FULTON, J. F. (1946), "Physiology of the Nervous System," 2nd edition. University Press, Oxford. Ch. XX.

HINES, M. (1944), "The Precentral Motor Cortex." University of Illinois Press. Ch. XVIII.

LEYTON, A. S. F., and SHERRINGTON, C. S. (1917), *Quart. J. Exper. Physiol.*, **11**, 137.

SHERRINGTON, C. S. (1906), "The Integrative Action of the Nervous System." Constable, London. Ch. IX.

——(1946), "The Endeavour of Jean Fernel." University Press, Cambridge, Pt. II

TOWER, S. (1940), *Brain*, **63**, 36.

——(1944), "The Precentral Motor Cortex." University of Illinois Press. Ch. VI.

WALSHE, F. M. R. (1942), *Brain*, **65**, 48.

WYSS, O. A. M., and OBRADOR, S. (1937), *Amer. J. Physiol.*, **120**, 42.

Notices of Recent Publications.

Prefrontal Leucotomy in 1,000 *Cases.* Report issued by the Board of Control. H.M. Stationery Office. 1947. Price sixpence.

The Board has issued this report in order to give "in broad outline" the experience of the operation of leucotomy in the hospitals under its control. It consists in a general introductory chapter explanatory of the design and aim of the operation, and of a statistical analysis and conclusions drawn therefrom.

This introduction is naïve to a degree. We read that "the prefrontal or forward part of the frontal lobe is concerned with thought, but its precise functions are obscure; it is very difficult to establish the relationship between such aspects of thought as imagination, initiative and self-consciousness on the one hand and any given part of the brain on the other." Yet if this psycho-anatomical miracle is not achieved, the operation nevertheless is designed to "break the connection between the patient's thoughts and his emotions," and it does this by severing the fronto-thalamic radiations and ensuring degeneration of the dorsomedial nucleus of the thalamus. We learn later, however, that the operation may yet be successful even when it achieves neither of these anatomical results, and it remains therefore an empirical procedure, producing its results—when it does—in an inexplicable fashion.

Those old enough to recall how ardently the late Dr. Charles Mercier campaigned for logic and clarity in psychiatric thought will be able to picture what his reaction would have been if he had been confronted with this confusion of psychological and anatomical categories.

All this, and such lush tautologies as "the tension of the urge to scrupulosity," will reveal the key in which this introduction is composed.

If the statistical part of the report is also disappointing, it is but fair to the authors to say that they are not responsible for the unsatisfactory nature of the material they were set to analyse, for it appears that the pre-operative and post-operative study and assessment of the case material conformed to no common standard of method and to no adequate standard of completeness. Thus, we read "it must be made clear that we have by no means fully analysed every case, because there was not full information on each. In any one record submitted to us there might be a great deal of detail or only a few words."

What, in brief, does their material allow of in the way of inferences ? (i) that prefrontal leucotomy consists in an incision into the frontal poles that may or may not sever the fronto-thalamic pathway, and may or may not lead to degenerative changes in the thalamus: that its clinical "success" may be just as great in the one case as in the other, and that in consequence it is an empirical procedure acting in an unknown way; (ii) that in a proportion (some 35 per cent.) of persons labelled schizophrenia, manic-depressive psychosis and obsessional neurosis, there ensues upon the operation an improvement in their symptoms allowing of their discharge from a mental hospital, and sometimes equivalent to full recovery. Of the precision and accuracy of diagnosis in this sample of 1,000 cases, of the details of their states before and after operation, we do not know.

It is probably not too much to say, from the general enthusiasm with which

psychiatrists have greeted this operation, that they have formed the impression that it is a very striking advance upon what they were able to achieve by orthodox psychiatric methods. Leucotomy promises that, when a more systematic pre- and post-operative study of cases submitted to it has been carried out, reliable indications for its use may be defined and the grounds of precise prognosis in any given instance may be made available.

But if this report does not satisfy us as a useful fulfilment of its difficult terms of reference, it teaches a lesson that probably neither the authors nor the Board of Control had in mind. It reveals in virtue of the very defects of its material how a generation of allegiance to doctrinal and allegorical medical psychologies has handicapped the average psychiatrist of to-day for labour in any field of scientific research where experimental or observational conditions have to be precisely formulated and controlled, where observation must be accurate, and methodically recorded as well as capable of repetition and verification. It reveals, too, how ill-placed an administrative body is to sponsor scientific investigation without expert guidance

The Normal Encephalogram. By Leo M. Davidoff and Cornelius J. Dyke. Second Edition. Henry Kimpton, London. 1946. Pp. 232. Price £1 7s. 6d.

The second edition of this monograph is based upon the study of more than 8,000 pneumoencephalograms. The death of Dr. Dyke has meant that the revision of the previous edition and the introduction of new material has been the work of Dr. Davidoff alone. The product of his work is an excellent publication which could be read with profit by all concerned in the making and interpretation of pneumoencephalograms.

In the first section of the book general considerations are fully discussed. These include the history of pneumoencephalography, its technique and the indications and contra-indications for the procedure. Postencephalographic reactions are discussed and observations on the causes of failure to obtain ventricular filling submitted. It is noteworthy that the authors favour the spinal rather than the cisternal route for the injection of the gas—and further that they consider that the whole procedure should be carried out in the X-ray department.

The second and larger part of the work deals with normal encephalographic anatomy under three headings. First the ventricles of the brain, secondly the subarachnoid channels and thirdly the intracranial structures outlined by the gas filled spaces. A large number of good reproductions of excellent X-ray films are included and where necessary useful plates illustrating the anatomy of the brain appended. This part of the book is a conscientious attempt to interpret pneumoencephalograms in terms of topographical anatomy. This anatomical study is pursued carefully and completely so that such structures as certain of the basal arteries and the oculomotor nerves are revealed on the films.

There is little deserving of adverse criticism here. From the anatomical point of view however it is not clear why the authors attempt to distinguish between the interventricular foramen and the foramen of Monro. To most of their readers these represent alternative names for the same structure and this would appear to be the usual anatomical view. The suggestion that there is a subarachnoid space beneath the sellar diaphragm is also at variance with the opinion of many anatomists. So too is the statement that the collateral eminence forms part of the lateral wall of the temporal horn of the lateral ventricle. Finally, at times, the

anatomical nomenclature is confusing. Such terms as "the ventral boundary of the third ventricle" leave one in doubt as to the region under discussion and in connection with such a cavity lucidity might be gained by referring to the superior, inferior, anterior and posterior boundaries.

This monograph is the result of a thoughtful analysis of a large experience of pneumoencephalography. The authors are to be congratulated on their work which will for long remain a standard reference on the subject.

Textbook of Clinical Neurology. By J. M. NIELSEN. Second Edition. Paul Hoeber Inc., New York. 1946. Price $7.50.

Readers old enough to recall the great clinical texts on neurology of the turn of the century, those of Gowers and Oppenheim, for example, will note with regret and misgiving that the "clinical" textbooks of our day become progressively less clinical, and now consist too largely of uncritical digests of animal physiology, applied electricity and some biochemistry. Clinical medicine fits in where it can find room.

No one could dispute that the growing employment of diagnostic and therapeutic procedures derived from the physical and biological sciences forces the textbook writer to cover an ever wider field. Too frequently, however, out of a false idea of scientific comprehensiveness, the reader is invited to know less and less about more and more, and he ends by being instructed neither clinically nor scientifically.

In these difficult circumstances, an author may be forgiven if he loses sight of first things, yet it remains an inexorable factor in the situation that the doctor's first approach to his task involves the skilled used of his trained senses, and a familiarity with the material of his labours, the sick patient. It must ever remain, therefore, a primary function of the "clinical" textbook to give the doctor all the aid that a written text can give.

It is surely of greater practical importance for the doctor to know the varied phenomena of an epileptic fit than to carry in his head all the latest technological details of electro-encephalography, and of greater use to him to be familiar with the main forms of paralysis and motor disorder than to have a smattering of information about that far from perfect science, cortical cytoarchitectonics. To know all about area 4S may be an engaging intellectual pastime for the practitioner, but it is wholly useless to him in the practice of his profession.

Surely, these are elementary considerations that the undergraduate student has the right to expect the writers of his texts to keep always in mind and to display on paper. Yet it is for this category that Professor Nielsen claims to be providing a systematized outline of "clinical" neurology. It is to be feared that with the ending of his preface he forgot his purpose and that he holds unpractical views as to how a student should be prepared for the practice of medicine.

In the clinical sections of the book we find a remarkable lack of any sense of proportion. Cervical rib is dismissed in ten uniquely uninformative lines, while in the same chapter a number of exceptionally rare disease conditions contain ampler notice.

The reader will look in vain for a really adequate account of hemiplegia, but he will get several pages on cortical architectonics. Similarly, Jacksonian epilepsy is summarily dealt with, but electro-encephalography has several pages.

If professors of clinical medicine adopt this perverse notion of medical education, we may well despair of the future of all clinical studies.